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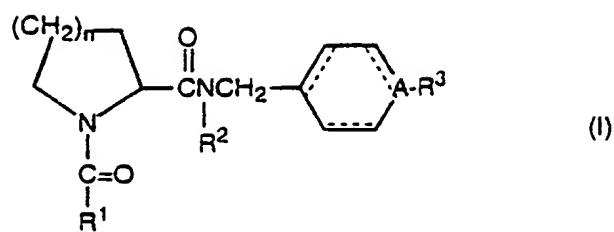
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㉚ Prolineamide derivatives.

㉛ A prolineamide derivative represented by the formula (I):



or a salt or hydrate thereof or a pharmaceutically acceptable salt thereof, which has a protease inhibition activity and is useful as an active ingredient of pharmaceutical compositions is provided.

FIELD OF THE INVENTION

5 The present invention relates to novel proline derivatives. More particularly, it relates to proline derivatives having a protease inhibition activity or pharmaceutically acceptable salts thereof and protease inhibitors containing the same as an active ingredient.

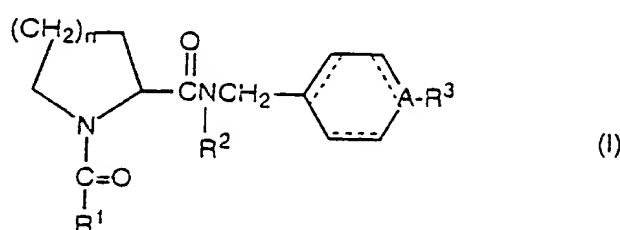
BACKGROUND OF THE INVENTION

10 It has been known that various proteases are present in the living body, for example, a group of serine proteases such as thrombin, factor Xa, factor IXa, factor VIIa, trypsin, plasmin, tissue plasminogen activator, kallikrein, C3/C5 convertase in the complement system, tryptase, etc. is known. Further, it is also known that these proteases cause various diseases when they are activated abnormally by some reason. Accordingly, substances which inhibit the activity of these proteases are useful as a clinical remedy. For example, antithrombin agents, anti-factor Xa agents and anti-factor VIIa agents are useful for treating thrombosis, 15 antitrypsin agents are useful for treating pancreatitis, antiplasmin agents are useful as hemostatics, antiallergic agents and antiinflammatory agents, anti-kallikrein agents are useful as a remedy for inflammation and ulcer, and anticomplementary agents are useful as a remedy for nephritis and rheumatoid arthritis. Protease inhibitors having these actions have hitherto been developed, but they are not necessarily sufficient for practical use in view of protease inhibition activity, stability in the living body and the like. For 20 example, tripeptide derivatives consist of arginine derivatives are known as protease inhibitors. That is, D-phenylalanyl-L-prolyl-L-arginal is known as a thrombin inhibitor (e.g. Folia Haematol., 109, 22 (1982)) but is fairly unstable in the living body (J. Med. Chem., 33, 1729 (1990)). Further, arginal derivatives (Japanese Laid-open Patent Publication No. 4-89498) or amidinophenylalanine derivatives (Thromb. Res., 17, 425 (1980)) are reported as protease inhibitors but their inhibition activity is low.

25 Under these circumstances, the present inventors have studied to develop structurally novel drugs having enzyme inhibition activity and stability in vivo, which are sufficient for practical use. As a result, it has been found that certain prolineamide derivatives can attain the desired object, thus the present invention has been established.

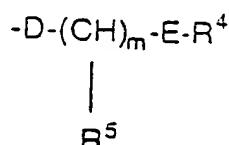
30 SUMMARY OF THE INVENTION

That is, the present invention provides a prolineamide derivative represented by the formula (I):



45 wherein A is a carbon atom or a nitrogen atom; n is an integer of 0 to 2; a broken line is absent or a single bond;
R¹ is

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55

{wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;
R⁴ is a C₁-C₆ alkyl group. -OR⁶ (R⁶ is a hydrogen atom, a C₁-C₆ alkyl group, an optionally substituted

5 C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group or an optionally substituted C_7 - C_{12} aralkyl group). $-SR^7$ (R^7 is a C_1 - C_6 alkyl group, an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group or an optionally substituted C_7 - C_{12} aralkyl group), $-SOR^8$ (R^8 is an optionally substituted C_6 - C_{10} aryl group or an optionally substituted C_3 - C_8 cycloalkyl group), $-SO_2R^9$ (R^9 is an optionally substituted C_6 - C_{10} aryl group or an optionally substituted C_3 - C_8 cycloalkyl group), $-COR^{10}$ (R^{10} is a hydroxyl group, a C_1 - C_6 alkoxy group, an optionally substituted C_6 - C_{10} aryl group or an optionally substituted C_3 - C_8 cycloalkyl group), $-NHR^{11}$ (R^{11} is a C_1 - C_6 alkyl group, an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group or an optionally substituted C_7 - C_{12} aralkyl group), $-NHCOR^{12}$ (R^{12} is a C_1 - C_6 alkoxy group, an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group or an optionally substituted C_7 - C_{12} aralkyl group), $-NHCO_2R^{13}$ (R^{13} is a C_1 - C_6 alkyl group, an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group, an optionally substituted C_7 - C_{12} aralkyl group, an optionally substituted 5- to 10-membered heterocyclic group), an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_3 - C_8 cycloalkyl group, an optionally substituted 5- to 10-membered heterocyclic group or $-SiR^{14}R^{15}R^{16}$ (R^{14} , R^{15} , and R^{16} independently indicate a C_1 - C_6 alkyl group);

10 R^6 is a $-OR^{17}$ (R^{17} is a hydrogen atom, $-SiR^{22}R^{23}R^{24}$ (R^{22} , R^{23} , and R^{24} independently indicate a C_1 - C_6 alkyl group), a C_1 - C_6 alkyl group or an optionally substituted 5- to 10-membered heterocyclic group), $-OCOR^{18}$ (R^{18} is a hydrogen atom, a C_1 - C_6 alkyl group, a C_1 - C_6 alkoxy group, an amino group, a C_1 - C_6 alkylamino group, a C_2 - C_{12} dialkylamino group or a C_2 - C_7 alkenylamino group), $-NHR^{19}$ (R^{19} is a hydrogen atom, a C_1 - C_6 alkyl group or an optionally substituted C_7 - C_{12} aralkyl group), $-NHCO_2R^{20}$ (R^{20} is a hydrogen atom, a C_1 - C_6 alkyl group, a C_1 - C_6 haloalkyl group, a C_1 - C_6 alkoxy group, an optionally substituted C_3 - C_8 cycloalkyl group, a C_2 - C_7 carboxyalkyloxy group, a C_2 - C_7 alkenyloxy group, an optionally substituted C_6 - C_{10} aryl group, an optionally substituted C_6 - C_{10} aryloxy group, a C_3 - C_9 alkoxy carbonylalkoxy group, a C_2 - C_{12} dialkylamino group or an optionally substituted C_7 - C_{12} aralkyloxy group) or $-NHCO_2R^{21}$ (R^{21} is a C_1 - C_6 alkyl group, a C_1 - C_6 haloalkyl group, a C_2 - C_7 carboxyalkyl group, an optionally substituted C_6 - C_{10} aryl group, a C_3 - C_9 alkoxy carbonylalkyl group or an optionally substituted C_7 - C_{12} aralkyl group); and m is 0 or 1;

15 R^2 is a hydrogen atom or a C_1 - C_6 alkyl group; and R^3 is $-C(=NR^{25})NH_2$ (R^{25} is a hydrogen atom, a C_1 - C_6 alkyl group, a C_2 - C_7 acyl group, a C_2 - C_7 acyloxy group, a C_1 - C_6 alkoxy group, a C_2 - C_7 alkoxy carbonyl group, a C_2 - C_7 alkoxy carbonyloxy group, a hydroxyl group or a C_2 - C_7 -hydroxyalkyl carbonyloxy group), $-NH-C(=NR^{25})NH_2$ (R^{25} is as defined above) or $-NHR^{25}$ (R^{25} is a hydrogen atom, a C_1 - C_6 alkyl group, a C_2 - C_7 acyl group, a C_2 - C_7 alkoxy carbonyl group or a 5- C_1 - C_3 alkyl-1,3-dioxol-2-on-4-ylmethyl group; provided that R^3 is $-C(=NR^{25})NH_2$ when A is a nitrogen atom or a salt and pharmaceutical use thereof.

35 DETAILED DESCRIPTION OF THE INVENTION

The prolineamide derivative of the present invention is represented by the above formula (I). Examples of the optionally branched C_1 - C_6 alkylene group in the above definition include $-CH_2-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-CH(CH_3)-$, $-C(CH_3)_2-$, $-CH(CH_3)CH_2-$, $-CH_2CH(CH_3)-$, $-C(CH_3)_2CH_2-$, $-CH_2C(CH_3)_2-$, $-CH(CH_3)CH(CH_3)-$ and the like. Examples of the C_1 - C_6 alkyl group include methyl group, ethyl group, n-propyl group, i-propyl group, n-butyl group, s-butyl group, i-butyl group, t-butyl group, n-pentyl group, n-hexyl group and the like. Examples of the C_1 - C_3 alkyl group include those having three carbon atoms or less among those illustrated above. Examples of the C_1 - C_6 alkoxy group include methoxy group, ethoxy group, n-propoxy group, i-propoxy group, n-butoxy group, s-butoxy group, i-butoxy group, t-butoxy group, n-pentyloxy group, n-hexyloxy group and the like. Examples of the C_2 - C_7 alkoxy carbonyl group include methoxycarbonyl group, ethoxycarbonyl group, n-propoxycarbonyl group, i-propoxycarbonyl group, n-butyloxycarbonyl group, t-butyloxycarbonyl group, n-pentyloxycarbonyl group, n-hexyloxycarbonyl group and the like. Examples of the C_3 - C_8 cycloalkyl group include cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group and the like. Examples of the C_6 - C_{10} aryl group include phenyl group, tolyl group, naphthyl group and the like. Examples of the C_7 - C_{12} aralkyl group include benzyl group, phenylethyl group, phenylpropyl group, naphthylmethyl group and the like. Examples of the C_6 - C_{10} aryloxy group include phenoxy group, naphthoxy group and the like. Examples of the C_7 - C_{12} aralkyloxy group include benzylxy group, phenylethoxy group, phenylpropoxy group, naphthylmethoxy group and the like. Examples of the heterocyclic group include those contain 1 to 4 heteroatoms selected from an oxygen atom, a sulfur atom and a nitrogen atom and the total number of atoms constituting the ring is 5 to 10, specifically, respective residues of furan ring, tetrahydrofuran ring, pyran ring, benzofuran ring, chroman ring, thiophene ring, benzothiophene ring, pyrrole ring, imidazole ring, pyrazole ring, triazole ring, pyridine ring, piperidine ring, pyrazine ring, piperazine ring, pyrimidine ring.

indole ring, benzimidazole ring, purine ring, quinoline ring, phthalazine ring, quinazoline ring, cinnoline ring, oxazole ring, thiazole ring, morpholine ring and the like. Examples of the C₁-C₆ haloalkyl group include chloromethyl group, bromomethyl group, dichloromethyl group, 1-chloroethyl group, 2-chloroethyl group, 3-chloropropyl group, 4-chlorobutyl group, 5-chloropentyl group, 6-chlorohexyl group, difluoromethyl group,

5 trifluoromethyl group and the like. Examples of the C₂-C₇ carboxyalkyl group include carboxymethyl group, 2-carboxyethyl group, 3-carboxypropyl group, 4-carboxybutyl group, 5-carboxypentyl group, 6-carboxyhexyl group and the like. Examples of the C₂-C₇ carboxyalkyloxy group include carboxymethoxy group, 2-carboxyethoxy group, 3-carboxypropoxy group, 4-carboxybutyloxy group, 5-carboxypentyloxy group, 6-carboxyhexyloxy group and the like. Examples of the C₂-C₇ alkenyloxy group include vinyloxy group, 10 aryloxy group, 2-propenyloxy group, isopropenyloxy group, 3-butenyloxy group, 4-pentenyloxy group, 5-hexenyloxy group and the like. Examples of the C₂-C₇ alkenylamino group include vinylamino group, 15 arylamino group, 2-propenylamino group, isopropenylamino group, 3-butenylamino group, 4-pentenylamino group, 5-hexenylamino group and the like. Examples of the C₁-C₆ alkylamino group include methylamino group, ethylamino group, n-propylamino group, n-butylamino group and the like. Examples of the C₂-C₁₂ 20 dialkylamino group include dimethylamino group, methylethylamino group, diethylamino group, di-n-propylamino group and the like. Examples of the C₂-C₇ acyl group include acetyl group, propionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group, pivaloyl group, hexanoyl group, heptanoyl group and the like. Examples of the C₂-C₇ acyloxy group include acyloxy group, propionyloxy group, butyryloxy group, isobutyryloxy group, valeryloxy group, isovaleryloxy group, pivaloyloxy group, hexanoxy group, heptanoyloxy group and the like. Examples of the C₂-C₇ alkoxy carbonyloxy group include methoxycarbonyloxy group, ethoxycarbonyloxy group, n-propoxycarbonyloxy group, n-butyloxycarbonyloxy group, n-pentyloxycarbonyloxy group, n-hexyloxycarbonyloxy group and the like. Examples of the C₂-C₇ 25 hydroxyalkylcarbonyloxy group include hydroxymethylcarbonyloxy group, 2-hydroxyethylcarbonyloxy group, 3-hydroxypropylcarbonyloxy group, 4-hydroxybutylcarbonyloxy group, 5-hydroxypentylcarbonyloxy group, 6-hydroxyhexylcarbonyloxy group and the like. Examples of the C₃-C₉ alkoxy carbonylalkoxy group include methoxycarbonylmethoxy group, ethoxycarbonylmethoxy group, propoxycarbonylmethoxy group, methoxycarbonylethoxy group, ethoxycarbonylethoxy group, propoxycarbonylethoxy group and the like. Examples of the C₃-C₉ 30 alkoxy carbonylalkyl group include methoxycarbonylmethyl group, ethoxycarbonylmethyl group, propoxycarbonylmethyl group, methoxycarbonylethyl group, methoxycarbonylmethyl group, propoxycarbonylethyl group and the like.

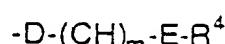
Examples of the substituent in the above definition of "optionally substituted (with substituent)" include above-described C₁-C₆ alkyl group; above-described C₁-C₆ haloalkyl group; above-described C₁-C₆ alkoxy group; hydroxyl group; carboxyl group; above-described C₂-C₇ carboxyalkyl group; above-described C₂-C₇ carboxyalkyloxy group; above-described C₂-C₇ acyl group; above-described C₂-C₇ acyloxy group; above-described C₂-C₇ alkoxy carbonyl group; above-described C₂-C₇ alkoxy carbonyloxy group; C₈-C₁₃ aralkyloxy carbonyl group such as benzyloxycarbonyl group, phenylethyoxy carbonyl group, phenylpropyloxycarbonyl group, naphthylmethyloxycarbonyl group, etc.; halogen atoms such as fluorine atom, chlorine atom, bromine atom and the like.

40 In the compound represented by the above formula (I), it is preferred that the 5- to 6-membered contains 1 to 4 heteroatoms selected from the group consisting of an oxygen atom, a sulfur atom and a nitrogen atom and the total number of atoms constituting the ring is 5 to 10. Further, as the substituent of the respective groups, a group(s) selected from C₁-C₆ alkyl group, C₁-C₆ haloalkyl group, C₁-C₆ alkoxy group, hydroxyl group, carboxyl group, C₂-C₇ carboxyalkyl group, C₂-C₇ carboxyalkyloxy group, C₂-C₇ acyl group, C₂-C₇ acyloxy group, C₂-C₇ alkoxy carbonyl group, C₂-C₇ alkoxy carbonyloxy group, C₈-C₁₃ aralkyloxy carbonyl group, C₃-C₉ alkoxy carbonylalkoxy group and halogen atoms is preferred.

45 In the compound represented by the above formula (I) of the present invention, a carbon atom is preferred as A.

Examples of preferred compounds of the present invention include those of the formula (I), wherein A is a carbon atom; n is 1 or 2; R¹ is

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(wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;

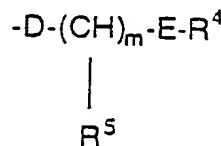
5 R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₁-C₆ alkyl group; a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group; or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonyloxy group, a C₃-C₉ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group, a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonyloxy group, a C₃-C₉ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group; or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonyloxy group, a C₃-C₉ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group; or a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonyloxy group, a C₃-C₉ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group); -COOH; a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxy carbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxy carbonyloxy group, a C₃-C₉ alkoxy carbonylalkoxy group and a benzyloxycarbonyl group; or a C₃-C₈ cycloalkyl group; or -SiR¹⁴R¹⁵R¹⁶ (R¹⁴, R¹⁵, and R¹⁶ independently indicate a C₁-C₆ alkyl group);

25 R⁸ is -OH, -OCOR¹⁸ (R¹⁸ is a C₁-C₆ alkoxy group or a C₂-C₇ alkenylamino group), -NH₂, -NHCOR²⁰ - (R²⁰ is a C₁-C₆ alkoxy group, a C₆-C₁₀ aryloxy group, a C₃-C₉ alkoxy carbonylalkoxy group, a C₂-C₁₂ dialkylamino group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group, a C₂-C₇ carboxyalkyl group, a C₆-C₁₀ aryl group, a C₃-C₉ alkoxy carbonylalkyl group or a C₇-C₁₂ aralkyl group); and m is 0 or 1};

30 R² is a hydrogen atom; and

35 R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom, a C₂-C₇ alkoxy carbonyl group or a hydroxyl group), -NH-C(=NR²⁵)NH₂ (R²⁵ is as defined above) or -NHR²⁶ (R²⁶ is a hydrogen atom, a C₂-C₇ alkoxy carbonyl group or a 5-C₁-C₃ alkyl-1,3-dioxol-2-on-4-ylmethyl group).

As the more preferred compound of the present invention, there is a compound of the formula (I), wherein A is a carbon atom; n is 1; R¹ is



(wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;

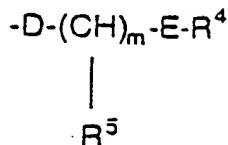
45 R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₆-C₁₀ aryl or C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group); a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group; or a C₁-C₆ cycloalkyl group;

50 R³ is -OH, -NH₂, -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group or a C₆-C₁₀ aryl group); and m is 1};

R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

55 As the more preferred compound of the present invention, there is a compound of the formula (I), wherein A is a carbon atom; n is 1; R¹ is



{wherein D is a single bond and E is a single bond or a C₁-C₆ alkylene group;

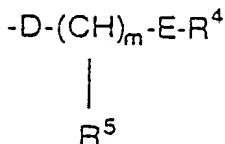
5 R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₆-C₁₀ aryl or C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group); a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group; or a C₃-C₆ cycloalkyl group;

10 15 R⁵ is -NH₂, -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group or a C₆-C₁₀ aryl group); and m is 1};

R² is a hydrogen atom; and

15 20 R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

As the still more preferred compound of the present invention, there is a compound of the formula (I), wherein A is a carbon atom; n is 1; R¹ is

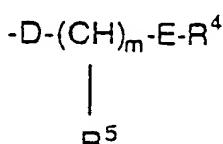


{wherein D is a single bond; E is a single bond or a C₁-C₃ alkylene group; R⁴ is a C₃-C₆ alkyl group, -OR⁶ (R⁶ is a C₁-C₆ alkyl group), a phenyl group or a C₃-C₆ cycloalkyl group; R⁵ is -OH, -NHR¹⁹ (R¹⁹ is a hydrogen atom), -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₃ alkyl group); and m is 1};

R² is a hydrogen atom; and

25 26 R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

As the particularly preferred compound of the present invention, there is a compound of the formula (I), wherein A is a carbon atom; n is 1; R¹ is



{wherein D is a single bond; E is a single bond or a C₁-C₆ alkylene group; R⁴ is a C₁-C₆ alkyl group; R⁵ is -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group); and m is 1};

R² is a hydrogen atom; and

45 50 R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group).

As the most preferred compound of the present invention, there is trans-4-[(S)-N-((R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl) prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 461 in Table 1 in Example 33).

The prolineamide derivatives represented by the above formula (I) can afford various stereoisomers. For example, concerning asymmetric carbon atoms, the absolute configuration may be D-configuration, L-configuration or DL configuration and all types thereof are included in the compounds of the present invention.

Examples of the salt which can be formed with the compounds of the above formula (I) of the present invention include inorganic acid salts such as hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, phosphate, etc.; organic acid salts such as succinate, oxalate, fumarate, maleate, lactate, tartrate, citrate, acetate, glycolate, methanesulfonate, toluenesulfonate, etc. Further, the proline derivatives of the above formula (I) containing a free carboxyl group can also form a salt with a pharmaceutically acceptable base.

5 Examples of the salt include alkaline metal salt, alkaline earth metal salt, ammonium salt, alkyl ammonium salt and the like.

Further, the prolineamide derivatives of the above formula (I) and the salts thereof can also form a hydrate.

10 Hereinafter, examples of the compounds of the present invention will be described.

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Table 1

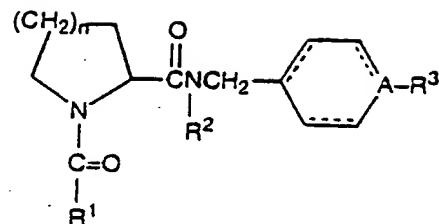


Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH_2)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
9	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{OCH}_3 \end{array} - CH_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
10	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{OCH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
11	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{OCH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
12	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{OCH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
13	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{Cl} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
14	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{Cl} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
15	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{Cl} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
16	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{F} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
17	$-(CH_2)_2 - \begin{array}{c} \text{C}_6\text{H}_4 \\ \\ \text{F} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	\AA	Broken line
18	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{F}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
19	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
20	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
21	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
22	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{OH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
23	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{OH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
24	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{OH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
25	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
26	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
27	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
28	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{CH}_2\text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
29	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{OCH}_2\text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
30	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COOCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
31	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COOCH}_2 - \text{C}_6\text{H}_4$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
32	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{COCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
33	$-\text{CH}_2 - \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
34	$-(CH_2)_2 - \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
35	$-(CH_2)_2 - \text{C}_6\text{H}_4 - \text{CH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
36	$-(CH_2)_2 - \text{C}_4\text{H}_3\text{S}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

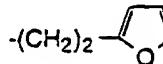
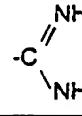
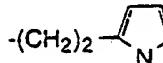
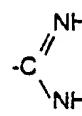
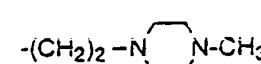
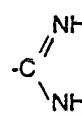
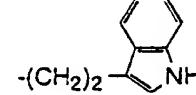
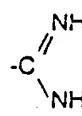
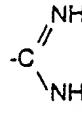
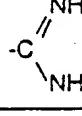
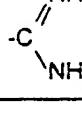
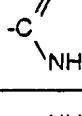
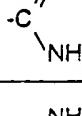
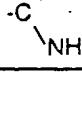
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
37	$-(CH_2)_2$ 	H		1	C	Single bond
38	$-(CH_2)_2$ 	H		1	C	Single bond
39	$-(CH_2)_2-N$ 	H		1	C	Single bond
40	$-(CH_2)_2$ 	H		1	C	Single bond
41	-CH ₃	H		1	C	Single bond
42	-CH ₂ CH ₃	H		1	C	Single bond
43	$-(CH_2)_2CH_3$	H		1	C	Single bond
44	-CH(CH ₃) ₂	H		1	C	Single bond
45	$-(CH_2)_3CH_3$	H		1	C	Single bond
46	-C(CH ₃) ₃	H		1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
47	$-(CH_2)_4CH_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
48	$-CH_2CH_2C(CH_3)_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
49	$-(CH_2)_9CH_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
50	$-CH_2Si(CH_3)_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
51	$-CH_2CH_2Si(CH_3)_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
52	$-CH_2OCH_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
53	$-CH_2O-\text{C}_6\text{H}_4-$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
54	$-CH_2O-\text{C}_6\text{H}_4-\text{H}$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
55	$-CH_2OCH_2-\text{C}_6\text{H}_4-$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
56	$-CH_2OH$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
57	$-CH_2SCH_3$	H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

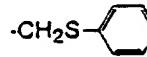
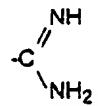
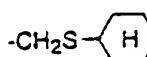
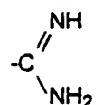
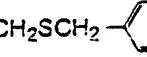
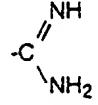
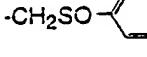
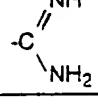
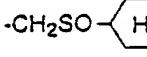
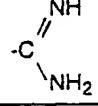
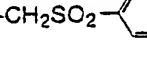
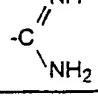
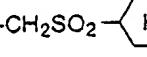
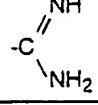
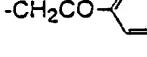
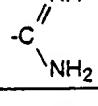
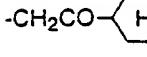
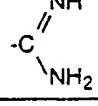
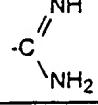
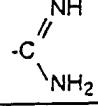
Compound No.	$\cdot R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$\cdot R^2$	$\cdot R^3$	n	A	Broken line
58	$\cdot CH_2S-$ 	-H		1	C	Single bond
59	$\cdot CH_2S-$ 	-H		1	C	Single bond
60	$\cdot CH_2SCH_2-$ 	-H		1	C	Single bond
61	$\cdot CH_2SO-$ 	-H		1	C	Single bond
62	$\cdot CH_2SO-$ 	-H		1	C	Single bond
63	$\cdot CH_2SO_2-$ 	-H		1	C	Single bond
64	$\cdot CH_2SO_2-$ 	-H		1	C	Single bond
65	$\cdot CH_2CO-$ 	-H		1	C	Single bond
66	$\cdot CH_2CO-$ 	-H		1	C	Single bond
67	$\cdot CH_2COOH$	-H		1	C	Single bond
68	$\cdot CH_2COOCH_3$	-H		1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
69	$-\text{CH}_2\text{NHCH}_3$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
70	$-\text{CH}_2\text{NH}-\text{C}_6\text{H}_5$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
71	$-\text{CH}_2\text{NH}-\text{C}_6\text{H}_4\text{H}_2$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
72	$-\text{CH}_2\text{NHCH}_2-\text{C}_6\text{H}_5$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
73	$-\text{CH}_2\text{NHCOOCH}_3$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
74	$-\text{CH}_2\text{NHCO}-\text{C}_6\text{H}_5$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
75	$-\text{CH}_2\text{NHCO}-\text{C}_6\text{H}_4\text{H}_2$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
76	$-\text{CH}_2\text{NHCOOCH}_2-\text{C}_6\text{H}_5$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
77	$-\text{CH}_2\text{NHSO}_2-\text{C}_4\text{H}_3\text{S}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
78	$-\text{CH}_2\text{NHSO}_2\text{CH}_3$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
79	$-\text{CH}_2\text{NHSO}_2-\text{C}_6\text{H}_5$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$\text{-R}_1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R_2	-R_3	n	A	Broken line
80	$-\text{CH}_2\text{NSO}_2\text{CH}_2-\text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
81	$-\text{CH}_2\text{NSO}_2-\text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
82	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
83	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ OH	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
84	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OSi}(\text{CH}_3)_3 \end{array} \text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
85	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ O-CH_3	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
86	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{O-} \text{C}_3\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
87	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OCHO} \end{array} \text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
88	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OCOCH}_3 \end{array} \text{C}_6\text{H}_5$	$-\text{H}$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
89	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OCOOCH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
90	$\begin{array}{c} -CH \\ \\ OCONH_2 \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
91	$\begin{array}{c} -CH \\ \\ OCONHCH_3 \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
92	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OCON(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
93	$\begin{array}{c} -CH_2CH \\ \\ OCONHCH_2CH=CH_2 \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
94	$\begin{array}{c} -CHCH_2 \\ \\ NHCHO \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
95	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOCH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
96	$\begin{array}{c} -CHCH_2 \\ \\ NHCOCF_3 \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
97	$\begin{array}{c} -CHCH_2 \\ \\ NHCOOCH_3 \\ \\ H \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
98	$-\text{CHC}(\text{SCH}_3)(\text{CH}_3)_2$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
99	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{NHCO-} \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
100	$-\text{CH}_2\text{CH} \begin{array}{c} \text{H} \\ \\ \text{NHCO-} \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
101	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOCH}_2\text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
102	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOCH}_2\text{CH=CH}_2 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
103	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOCH}_2\text{COOH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
104	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
105	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R_5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
106	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
107	$\begin{array}{c} -CH- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
108	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
109	$\begin{array}{c} -CH(CH_2)_3CH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
110	$\begin{array}{c} -CHCH_2CH_2SCH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
111	$\begin{array}{c} -CH_2CH- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
112	$\begin{array}{c} -CHCH_2CH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
113	$\begin{array}{c} -CHCH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
114	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
115	$\begin{array}{c} -CHCH(CH_3)CH_2CH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
116	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4-\text{F} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
117	$\begin{array}{c} -CH(CH_2)_4\text{COOEt} \\ \\ \text{NHSO}_2\text{Me} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
118	$\begin{array}{c} -CH(CH_2)_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOCH}_2- \text{C}_6\text{H}_4- \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
119	$\begin{array}{c} -CH(CH_2)_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
120	$\begin{array}{c} -CH(CH_2)_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
121	$\begin{array}{c} -CHCH_2O- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOCH}_2- \text{C}_6\text{H}_4- \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
122	$\begin{array}{c} -CHCH_2O- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
123	$\begin{array}{c} -CHCH_2O- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$ $\begin{array}{c} \text{COOCH}_2- \text{C}_6\text{H}_4- \\ \\ \text{COOCH}_2- \text{C}_6\text{H}_4- \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
124	$\begin{array}{c} -CHCH_2O- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{COOH} \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
125	$\begin{array}{c} -CHCH_2CH_2- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{Cl} \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
126	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{COOCH}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{COOH} \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
127	$\begin{array}{c} -CHCH_2CH_2- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{COOCH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
128	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{COOH} \\ \\ \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
129	$\begin{array}{c} -CHCH_2O- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
130	$\begin{array}{c} -CHCH_2O- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{COOH} \\ \\ \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
131	$\begin{array}{c} -CHCH_2O- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{COOCH}_2- \\ \\ \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
132	$\begin{array}{c} -CHCH_2S-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
133	$\begin{array}{c} -CHCH_2S-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
134	$\begin{array}{c} \text{CF}_3 \\ \\ -CHCH_2S-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
135	$\begin{array}{c} \text{H} \\ \\ -CH-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4-\text{OCH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
136	$\begin{array}{c} \text{H} \\ \\ -CHCH_2-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4-\text{OCH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
137	$\begin{array}{c} \text{H} \\ \\ -CH-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4-\text{OCH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
138	$\begin{array}{c} \text{H} \\ \\ -CHCH_2-\text{C}_6\text{H}_4-\text{OCH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4-\text{OCH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
139	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4-\text{CH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
140	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4-\text{OH} \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
141	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4-\text{COOH} \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
142	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
143	$\begin{array}{c} -CHCH_2\text{OCH}_3 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
144	$\begin{array}{c} -CHCH_2\text{O}-\text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
145	$\begin{array}{c} -CHCH_2\text{O}-\text{C}_6\text{H}_4-\text{COOH} \\ \\ \text{NHSO}_2-\text{C}_6\text{H}_4 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
146	$\begin{array}{c} -CHCH_2SCH_3 \\ \\ NHSO_2- \text{C}_6\text{H}_4- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
147	$\begin{array}{c} -CHCH_2S- \text{C}_6\text{H}_4- \text{C}_6\text{H}_5 \\ \\ NHSO_2- \text{C}_6\text{H}_4- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
148	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \text{H} \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
149	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \text{H} \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
150	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \text{OH} \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
151	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
152	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
153	$\begin{array}{c} -CHCH_2O- \text{C}_6\text{H}_4- \text{H} \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
154	$\begin{array}{c} -CHCH_2O- \text{C}_6\text{H}_4- \text{H} \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

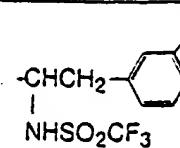
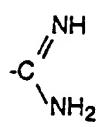
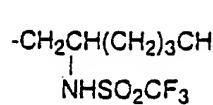
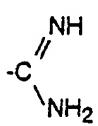
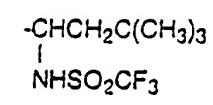
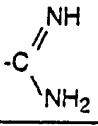
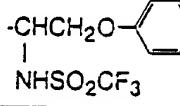
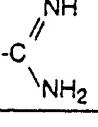
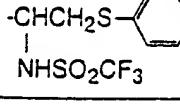
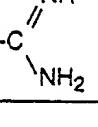
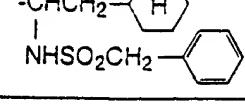
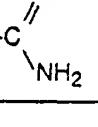
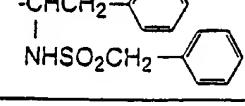
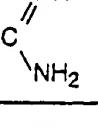
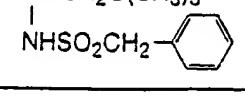
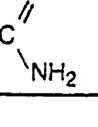
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
155	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_2\text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
156	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_2\text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
157	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
158	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
159	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{CH}_3-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
160	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{OCH}_3-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
161	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{F}-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
162	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{COOH}-\text{NHSO}_2\text{CF}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
163		-H		1	C	Single bond
164		-H		1	C	Single bond
165		-H		1	C	Single bond
166		-H		1	C	Single bond
167		-H		1	C	Single bond
168		-H		1	C	Single bond
169		-H		1	C	Single bond
170		-H		1	C	Single bond

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Table 1 (continued)

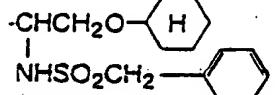
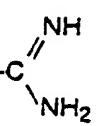
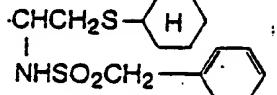
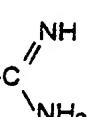
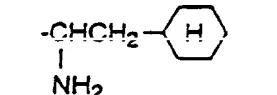
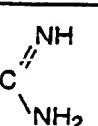
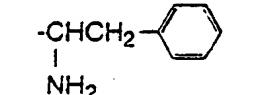
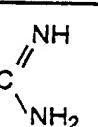
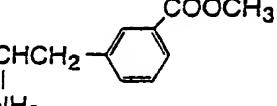
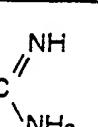
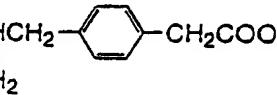
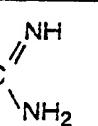
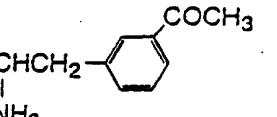
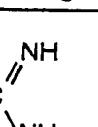
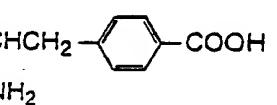
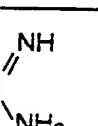
Compound No.	$-R^1 \left(-D-(CH)_m-E-R^4 \right)$	-R2	-R3	n	A	Broken line
171		-H		1	C	Single bond
172		-H		1	C	Single bond
173		-H		1	C	Single bond
174		-H		1	C	Single bond
175		-H		1	C	Single bond
176		-H		1	C	Single bond
177		-H		1	C	Single bond
178		-H		1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
179	$-\text{CH}(\text{CH}_2)_4\text{CH}_3$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
180	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
181	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_5$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
182	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_4-\text{OH}$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
183	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_5$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
184	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_5$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
185	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_4-\text{Cl}$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
186	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_5$ NH_2	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
187	$-\text{CH}-\text{C}_6\text{H}_5$ NHCH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ \text{-C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
188	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_2\text{C}_2\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
189	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
190	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{OCH}_2\text{COOH}$ $-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
191	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{COOH}$ $-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
192	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
193	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
194	$-\text{CHCH}_2\text{S}-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
195	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_2-\text{C}_6\text{H}_4-\text{NHCH}_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -O-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
196	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHCH_2- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
197	$\begin{array}{c} -CH_2CH(CH_2)_3CH_3 \\ \\ NHCH_2- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
198	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCH_2- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
199	$\begin{array}{c} -CHCH_2OC_2H_5 \\ \\ NHCH_2- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
200	$\begin{array}{c} -CHCH_2SCH_3 \\ \\ NHCH_2- \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
201	C_6H_5	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	—
202	$\text{CH}_2- \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	—
203	$\text{CH}_2- \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	—
204	$-(CH_2)_2CH_3$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
205	<chem>-CH2Oc1ccccc1</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
206	<chem>-CH2Oc1ccccc1C</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
207	<chem>-CH2Oc1ccccc1OC</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
208	<chem>-CH2Oc1ccccc1Cl</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
209	<chem>-CH2Oc1ccccc1C(F)(F)F</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
210	<chem>-CH2Oc1ccccc1O</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
211	<chem>-CH2Oc1ccccc1CC(=O)O</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
212	<chem>-CH2Oc1ccccc1CC(=O)O</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—
213	<chem>-CH2Oc1ccccc1C(=O)O</chem>	-H	<chem>N=C(N)C(=O)N</chem>	1	C	—

Table 1 (continued)

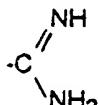
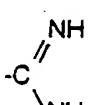
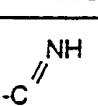
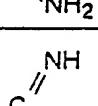
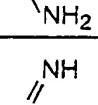
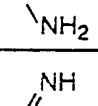
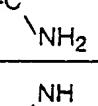
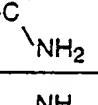
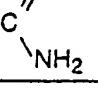
Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R_5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
214	$-\text{CH}_2\text{O}-\text{C}_6\text{H}_4-\text{COOCH}_3$	-H		1	C	—
215	$-\text{CH}_2\text{O}-\text{C}_6\text{H}_4-\text{COOCH}_2$	-H		1	C	—
216	$-\text{CH}_2\text{O}-\text{C}_6\text{H}_4-\text{COCH}_3$	-H		1	C	—
217	$-\text{CH}_2\text{S}-\text{C}_6\text{H}_4$	-H		1	C	—
218	$-\text{CH}_2\text{S}-\text{C}_6\text{H}_4-\text{OH}$	-H		1	C	—
219	$-\text{CH}_2\text{S}-\text{C}_6\text{H}_4-\text{COOH}$	-H		1	C	—
220	$-\text{CH}_2\text{S}-\text{C}_6\text{H}_4-\text{COCH}_3$	-H		1	C	—
221	$-\text{CH}(\text{H})-\text{C}_6\text{H}_4-\text{OH}$	-H		1	C	—
222	$-\text{CH}(\text{OCOCH}_3)-\text{C}_6\text{H}_4$	-H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
223	$\begin{array}{c} -CHCH_2- \\ \\ OCOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
224	$\begin{array}{c} -CHCH_2- \\ \\ OCOOCH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
225	$\begin{array}{c} -CHCH_2- \\ \\ NHCHO \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
226	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
227	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
228	$\begin{array}{c} -CH \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
229	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH_2- \\ \\ C_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
230	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
231	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2 \text{C}_2\text{H}_5 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
232	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2 \text{-} \text{C}_6\text{H}_5 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
233	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2 \text{COOH} \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
234	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NH}_2 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
235	$\text{-CH} \text{-} \begin{array}{c} \text{H}_5\text{C}_6 \\ \\ \text{OH} \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
236	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H}_5\text{C}_6 \\ \\ \text{OH} \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
237	$\text{-CH} \text{-} \begin{array}{c} \text{H}_5\text{C}_6 \\ \\ \text{NHSO}_2 \text{CH}_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
238	$\text{-CH} \text{-} \begin{array}{c} \text{H}_5\text{C}_6 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

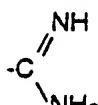
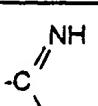
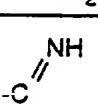
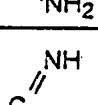
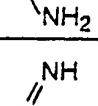
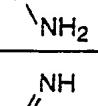
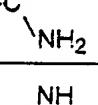
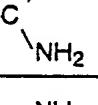
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
239	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	H		1	C	—
240	$\begin{array}{c} -CHCH_2OC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H		1	C	—
241	$\begin{array}{c} -CHCH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	H		1	C	—
242	$\begin{array}{c} -CHCH(CH_3)_2 \\ \\ NHCOOC_2H_5 \end{array}$	H		1	C	—
243	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	H		1	C	—
244	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H		1	C	—
245	$\begin{array}{c} -CH(CH_2)_3CH_3 \\ \\ NHSO_2CH_3 \end{array}$	H		1	C	—
246	$\begin{array}{c} -CHCH_2CH_2SCH_3 \\ \\ NHSO_2CH_3 \end{array}$	H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
247	$\begin{array}{c} -CHCH_2- \\ \\ OCOCH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
248	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
249	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
250	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
251	$\begin{array}{c} -CHCH_2CH_2- \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
252	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2- \\ \\ \text{C}_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
253	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_2COOH \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
254	$\begin{array}{c} -CH_2CH- \\ \\ NHCHO \end{array}$	-H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
255	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4-\text{F} \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
256	$\begin{array}{c} \text{CH}_3 \\ \\ -CHCH_2-\text{C}_6\text{H}_4-\text{CH}_2-\text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
257	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NH}_2 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
258	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
259	$\begin{array}{c} -\text{CH}(\text{CH}_2)_4\text{CH}_3 \\ \\ \text{OCOCH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
260	$\begin{array}{c} -\text{CHC}(\text{SCH}_3)(\text{CH}_3)_2 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
261	$\begin{array}{c} -\text{CHCH}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OCONHCH}_2\text{CH}=\text{CH}_2 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
262	$\begin{array}{c} -\text{CH}(\text{CH}_2)_3\text{CH}_3 \\ \\ \text{NHCOOCH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
263	$\begin{array}{c} -\text{CHCH}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(-D-(CH)_m-E-R^4 \right)$	-R ₂	-R ₃	n	A	Broken line
264	$\begin{array}{c} -CH_2CH(C_2H_5)_2 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
265	$\begin{array}{c} -CH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
266	$\begin{array}{c} -CH_2C(CH_3)_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
267	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOCH_2-\text{C}_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
268	$\begin{array}{c} -CH_2CH(CH_2)_2CH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
269	$\begin{array}{c} -CH_2CH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
270	$\begin{array}{c} -CH_2C(CH_3)_3 \\ \\ NHSO_2-\text{C}_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
271	$\begin{array}{c} -CH_2CH(CH_2)_2CH_3 \\ \\ NH_2 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
272	$-(CH_2)_2-\text{C}_6H_5$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	N	—
273	$-CH_2OCH_2-\text{C}_6H_5$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	N	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
274	$-CH \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
275	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHCHO} \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
276	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
277	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
278	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{NH}_2 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
279	$-CH_2\text{CH} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
280	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{OCOOC}_2\text{H}_5 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
281	$-CH\text{CH}_2 \begin{array}{c} \text{---} \\ \\ \text{OCONHCH}_2\text{CH=CH}_2 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—

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Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-} \text{R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
282	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{OH} \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
283	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
284	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
285	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
286	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
287	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
288	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—
289	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array} \text{---} \text{C}_6\text{H}_5$	H	$\text{-C} \begin{array}{c} \text{---} \\ \text{NH} \\ \parallel \\ \text{NH}_2 \end{array}$	1	N	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
290	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
291	$-\text{CHCH}_2 \begin{array}{c} \text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
292	$-\text{CH}(\text{CH}_2)_2\text{SCH}_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
293	$-\text{CH}(\text{CH}_2)_3\text{CH}_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
294	$-\text{CHC}(\text{SCH}_3)(\text{CH}_3)_2$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
295	$-\text{CH}(\text{CH}_2)_4\text{CH}_3$ $\text{NHSO}_2\text{CH}_2\text{COOH}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
296	$-\text{CHCH}_2 \begin{array}{c} \text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
297	$-\text{CHCH}_2 \begin{array}{c} \text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
298	$-\text{CHCH}_2 \begin{array}{c} \text{CH}(\text{C}_2\text{H}_5)_2 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
299	$-\text{CHCH}_2 \begin{array}{c} \text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ // \\ -\text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -O-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
300	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH_2 \text{---} \text{C}_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	N	—
301	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OH \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	N	—
302	$\begin{array}{c} -CH(CH_2)_2COOH \\ \\ NHSO_2 \text{---} \text{C}_6H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	N	—
303	$\begin{array}{c} -CH \text{---} \text{C}_6H_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond
304	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond
305	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6H_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond
306	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6H_5 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond
307	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond
308	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6H_5 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	2	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
309	$-(CH_2)_3 - \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
310	$-\text{CHCH}_2 - \text{C}_6\text{H}_5$ NH ₂	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
311	$-\text{CH} - \text{C}_6\text{H}_5$ NHCOOCH(CH ₃) ₂	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
312	$-\text{CHCH}_2 \text{C}(\text{C}_2\text{H}_5)_2$ NHCOOC(CH ₃) ₃	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
313	$-\text{CHCH}_2 \text{C}(\text{CH}_3)_3$ OH	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
314	$-\text{CH}_2 \text{CH} - \text{C}_6\text{H}_5$ NHSO ₂ CH ₃	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
315	$-\text{CHCH}_2 - \text{C}_6\text{H}_5$ OCOOC ₂ H ₅	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
316	$-\text{CH} - \text{C}_6\text{H}_5$ OH	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
317	$-\text{CHCH}_2 - \text{C}_6\text{H}_5$ NHSO ₂ CH ₃	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
318	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
319	$\begin{array}{c} -CH\text{CH}_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
320	$\begin{array}{c} -CH\text{CH}_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
321	$\begin{array}{c} -CH\text{CH}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
322	$\begin{array}{c} -CH\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)_2 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
323	$\begin{array}{c} -CH\text{CH}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	—
324	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	N	—
325	$\begin{array}{c} -CH\text{CH}_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	N	—
326	$\begin{array}{c} -CH\text{CH}_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	N	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
327	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	2	N	—
328	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	2	N	—
329	$\begin{array}{c} -\text{CH}(\text{CH}_2)_2\text{SCH}_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	2	N	—
330	$\begin{array}{c} -\text{CHCH}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OH} \end{array}$	H	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	2	N	—
331	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
332	$\begin{array}{c} -CH-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
333	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
334	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-CH ₃	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond
335	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OH} \end{array}$	-CH ₃	$\begin{array}{c} \text{NH} \\ \parallel \\ -C \\ \backslash \quad / \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

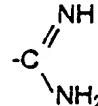
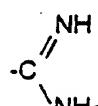
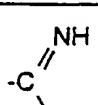
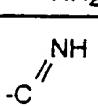
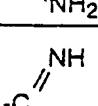
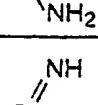
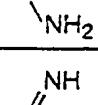
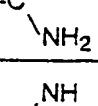
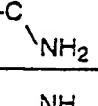
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
336	$-\text{CHCH}_2\text{CH}(\text{C}_2\text{H}_5)_2$ $\text{NHCOOC}(\text{CH}_3)_3$	$-\text{CH}_3$		1	C	Single bond
337	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	$-\text{CH}_3$		1	C	Single bond
338	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	$-\text{CH}_3$		1	C	—
339	$-\text{CH}-\text{C}_6\text{H}_5$ $\text{NHCOOCH}(\text{CH}_3)_2$	$-\text{CH}_3$		1	C	—
340	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	$-\text{CH}_3$		1	C	—
341	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_5$ OCOOC_2H_5	$-\text{CH}_3$		1	C	—
342	$-\text{CHCH}_2\text{CH}(\text{C}_2\text{H}_5)_2$ $\text{NHCOOC}(\text{CH}_3)_3$	$-\text{CH}_3$		1	C	—
343	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	$-\text{CH}_3$		1	C	—
344	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ OH	$-\text{CH}_3$		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
345	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
346	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_4-\text{NHCOOCH}(\text{CH}_3)_2$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
347	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
348	$-\text{CH}-\text{C}_6\text{H}_4-\text{OCOOC}_2\text{H}_5$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
349	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
350	$-\text{CHCH}_2\text{CH}(\text{C}_2\text{H}_5)_2-\text{NHCOOC}(\text{CH}_3)_3$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
351	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3-\text{OH}$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	N	—
352	$-\text{CH}-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond
353	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOCH}(\text{CH}_3)_2$	$-\text{CH}_3$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	2	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
354	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	Single bond
355	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_4-\text{OCOOC}_2\text{H}_5$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	Single bond
356	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	Single bond
357	$-\text{CH}(\text{CH}_2)_4\text{CH}_3-\text{NHCOOC}(\text{CH}_3)_3$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	Single bond
358	$-\text{CHCH}_2\text{CH}(\text{CH}_3)_2-\text{OH}$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	Single bond
359	$-\text{CH}-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	—
360	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOC}_2\text{H}_5$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	—
361	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	—
362	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_4-\text{OCOOC}(\text{CH}_3)_2$	$-\text{CH}_3$	$-\text{C} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	2	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
363	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	C	—
364	$\begin{array}{c} -CHC(SCH_3)(CH_3)_2 \\ \\ NHCOOC(CH_3)_3 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	C	—
365	$\begin{array}{c} -CHCH_2CH(CH_3)_3 \\ \\ NH_2 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	C	—
366	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHCOOC_2H_5 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
367	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
368	$\begin{array}{c} -CH-\text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
369	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4-COOH \\ \\ OCOOCH(CH_3)_2 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
370	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_2COOH \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
371	$\begin{array}{c} -CH(CH_2)_2SCH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—
372	$\begin{array}{c} -CH_2CH(CH_2)_3CH_3 \\ \\ OH \end{array}$	$-CH_3$	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	2	N	—

Table 1 (continued)

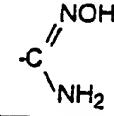
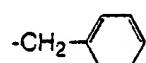
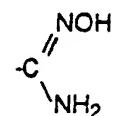
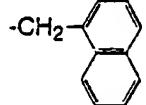
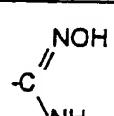
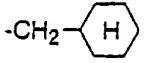
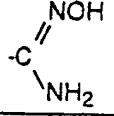
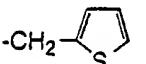
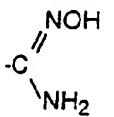
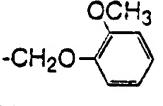
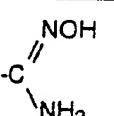
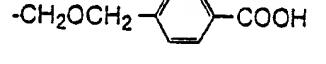
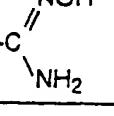
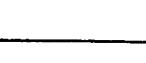
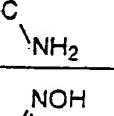
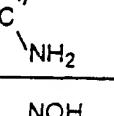
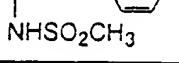
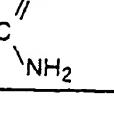
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
373		-H		1	C	Single bond
374		-H		1	C	Single bond
375		-H		1	C	Single bond
376		-H		1	C	Single bond
377		-H		1	C	Single bond
378		-H		1	C	Single bond
379		-H		1	C	Single bond
380		-H		1	C	Single bond
381		-H		1	C	Single bond
382		-H		1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
383	$\begin{array}{c} -CHCH_2- \\ \\ OH \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
384	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
385	$\begin{array}{c} -CHCH_2- \\ \\ OCOOCH(CH_3)_2 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
386	$\begin{array}{c} -CH_2CH- \\ \\ NHCHO \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
387	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC_2H_5 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
388	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH(CH_3)_2 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
389	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC(CH_3)_3 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond
390	$\begin{array}{c} -CHCH_2- \\ \\ NH_2 \end{array} \text{---} \begin{array}{c} \text{C}_6\text{H}_5 \\ \end{array}$	H	$\begin{array}{c} NOH \\ \parallel \\ -C \\ \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
391	$\begin{array}{c} -CH- \\ \\ OH \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
392	$\begin{array}{c} -CHCH_2- \\ \\ OCOCH_3 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
393	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
394	$\begin{array}{c} -CH- \\ \\ NHCOOC_2H_5 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
395	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH(CH_3)_2 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
396	$\begin{array}{c} -CH- \\ \\ NHCOOC(CH_3)_3 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
397	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC(CH_3)_3 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
398	$\begin{array}{c} -CH- \\ \\ NHSO_2CH_3 \end{array} \begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
399	$-CHCH_2 \begin{array}{c} \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
400	$-CHCH_2 \begin{array}{c} \\ \text{NH}_2 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
401	$-CH \begin{array}{c} \\ \text{OH} \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
402	$-CH \begin{array}{c} \\ \text{NH}_2 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
403	$-CH \begin{array}{c} \\ \text{NHCOOC}_2\text{H}_5 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
404	$-CH \begin{array}{c} \\ \text{NHCOOC(CH}_3)_3 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
405	$-CHCH_2\text{CH}(\text{CH}_3)_2 \begin{array}{c} \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
406	$-CHCH_2\text{CH}(\text{CH}_3)_2 \begin{array}{c} \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
407	$-CHCH(\text{CH}_3)_2 \begin{array}{c} \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
408	$\begin{array}{c} -CHCH(CH_3)_2 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
409	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
410	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
411	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
412	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
413	$\begin{array}{c} -CHCH_2CH_2SCH_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
414	$\begin{array}{c} -CHCH_2CH_2SCH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
415	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ OCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
416	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
417	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
418	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
419	$\begin{array}{c} -CHC(SCH_3)(CH_3)_2 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	Single bond
420	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	Single bond
421	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NH_2 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	Single bond
422	$\begin{array}{c} -CH \\ \\ OH \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—
423	$\begin{array}{c} -CHCH_2 \\ \\ OCOCH_3 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—
424	$\begin{array}{c} -CHCH_2 \\ \\ OCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—
425	$\begin{array}{c} -CH \\ \\ NH_2 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—
426	$\begin{array}{c} -CHCH_2 \\ \\ NH_2 \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—
427	$\begin{array}{c} -CH \\ \\ NHCHO \end{array}$	H	$\begin{array}{c} NOH \\ \diagup \\ -C \\ \diagdown \\ NH_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
428	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
429	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
430	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
431	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
432	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
433	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
434	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
435	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(-O-(CH)_m-E-R^4 \right)$ R^5	-R2	-R3	n	A	Broken line
436		H		1	C	—
437		H		1	C	—
438		H		1	C	—
439		H		1	C	—
440		H		1	C	—
441		H		1	C	—
442		H		1	C	—
443		H		1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
444	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NH}_2$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
445	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_4-\text{OCOCH}_3$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
446	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{OCOOC}_2\text{H}_5$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
447	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOC}_2\text{H}_5$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
448	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOCH}(\text{CH}_3)_2$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
449	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
450	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOCH}_2-\text{C}_6\text{H}_4$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
451	$-\text{CH}_2\text{CH}-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	-H	$-\text{C} \begin{array}{c} \text{NOH} \\ // \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
452	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
453	$\begin{array}{c} -CH(CH_2)_4\text{CH}_3 \\ \\ \text{OH} \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
454	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OH} \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
455	$\begin{array}{c} -CHCH_2\text{CH}(\text{C}_2\text{H}_5)_2 \\ \\ \text{OCOCH}_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
456	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
457	$\begin{array}{c} -\text{CH}_2\text{CH}(\text{CH}_2)_2\text{CH}_3 \\ \\ \text{NHCHO} \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
458	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH}_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
459	$\begin{array}{c} -CH(CH_2)_4\text{CH}_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
460	$\begin{array}{c} -CHCH_2\text{CH}(\text{C}_2\text{H}_5)_2 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
461	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

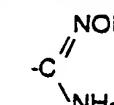
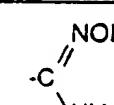
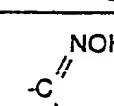
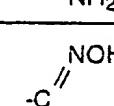
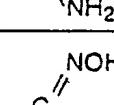
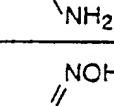
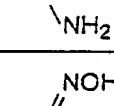
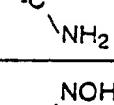
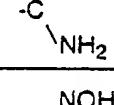
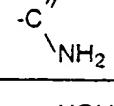
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
462	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H		1	C	—
463	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H		1	C	—
464	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H		1	C	—
465	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H		1	C	—
466	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H		1	C	—
467	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H		1	C	—
468	$\begin{array}{c} -CH(CH_2)_2SCH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H		1	C	—
469	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH_2\text{C}_6H_5 \end{array}$	-H		1	C	—
470	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NH_2 \end{array}$	-H		1	C	—
471	$\begin{array}{c} -CH\text{C}_6H_5 \\ \\ NHCOOC_2H_5 \end{array}$	-H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
472	$\begin{array}{c} -CH \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
473	$\begin{array}{c} -CHCH_2CH(CH}_3)_2 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
474	$\begin{array}{c} -CHCH_2CH(CH}_3)_2 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
475	$\begin{array}{c} -CH(CH_2)_2CH_3 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
476	$\begin{array}{c} -CH(CH_2)_2CH_3 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
477	$\begin{array}{c} -CHCH(CH}_3)_2 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
478	$\begin{array}{c} -CHCH(CH}_3)_2 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
479	$\begin{array}{c} -CHC(CH}_3)_3 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
480	$\begin{array}{c} -CHC(CH}_3)_3 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
481	$\begin{array}{c} -CHCH_2\text{Si(CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -C \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
482	$-\text{CHCH}_2\text{Si}(\text{CH}_3)_3$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
483	$-\text{CHCH}_2\text{CH}_2\text{SCH}_3$ $\quad $ $\quad \text{NHCOOC}_2\text{H}_5$	H		1	C	—
484	$-\text{CHCH}_2\text{CH}_2\text{SCH}_3$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
485	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_3$ $\quad $ $\quad \text{NHCOOC}_2\text{H}_5$	H		1	C	—
486	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_3$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
487	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ $\quad $ $\quad \text{NHCOOC}_2\text{H}_5$	H		1	C	—
488	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
489	$-\text{CHCH}_2\text{OC}(\text{C}_2\text{H}_5)_2\text{CH}_3$ $\quad $ $\quad \text{NHCOOC}_2\text{H}_5$	H		1	C	—
490	$-\text{CHCH}_2\text{OC}(\text{C}_2\text{H}_5)_2\text{CH}_3$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
491	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$ $\quad $ $\quad \text{NHCOOCH}(\text{CH}_3)_2$	H		1	C	—
492	$-\text{CHCH}_2\text{SC}(\text{CH}_3)_3$ $\quad $ $\quad \text{NHCOOC}_2\text{H}_5$	H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
493	$-\text{CHCH}_2\text{SC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ $\text{NHCOOC}_2\text{H}_5$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
494	$-\text{CHCH}_2\text{SC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ $\text{NHCOOCH}(\text{CH}_3)_2$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
495	$-\text{CHC}(\text{CH}_3)_2\text{SC}_2\text{H}_5$ $\text{NHCOOC}_2\text{H}_5$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
496	$-\text{CHC}(\text{CH}_3)_2\text{SC}_2\text{H}_5$ $\text{NHCOOCH}(\text{CH}_3)_2$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
497	$-\text{CHC}(\text{CH}_3)_2\text{SCH}(\text{CH}_3)_2$ $\text{NHCOOC}_2\text{H}_5$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
498	$-\text{CHC}(\text{CH}_3)_2\text{SCH}(\text{CH}_3)_2$ $\text{NHCOOCH}(\text{CH}_3)_2$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
499	$-\text{CHC}(\text{CH}_3)_2\text{SCH}(\text{C}_2\text{H}_5)_2$ $\text{NHCOOC}_2\text{H}_5$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
500	$-\text{CHC}(\text{CH}_3)_2\text{SCH}(\text{C}_2\text{H}_5)_2$ $\text{NHCOOCH}(\text{CH}_3)_2$	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
501	$-\text{CH}(\text{CH}_2)_4\text{CH}_3$ NHSO_2CH_3	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
502	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
503	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHSO_2 \text{---} \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
504	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2 \text{---} \text{C}_6\text{H}_4 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
505	$\begin{array}{c} -CH \text{---} \text{C}_6\text{H}_4 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
506	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_4 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
507	$\begin{array}{c} -CH_2CH \text{---} \text{C}_6\text{H}_4 \\ \\ NH_2 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
508	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_4 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
509	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
510	$\begin{array}{c} -CH(CH_2)_2SCH_3 \\ \\ NHSO_2CH_3 \end{array}$	H	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	N	—
511	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_4 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-CH ₃	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
512	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-CH ₃	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	Single bond
513	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-CH ₃	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	Single bond
514	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-CH ₃	$\begin{array}{c} \text{NOH} \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	2	C	Single bond
515	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
516	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
517	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
518	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
519	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
520	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ // \\ -C \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
521	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	Single bond
522	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOCH}(\text{CH}_3)_2$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	Single bond
523	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	Single bond
524	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ OH	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	Single bond
525	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	—
526	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	—
527	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	—
528	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	—
529	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \parallel \\ \text{C} \\ \backslash \text{NH}_2 \end{array}$	1	C	—

50

55

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
530	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ OH \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
531	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
532	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
533	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
534	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OH \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
535	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
536	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
537	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
538	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -O-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
539	$\begin{array}{c} -CHCH_2CH(CH_3)_2 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NOCOOCH_3 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	—
540	$\begin{array}{c} -CHCH_2CH(CH_3)_2 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOCOOCH_3 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	—
541	$\begin{array}{c} -CH \\ \\ NHCOOC(CH_3)_3 \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
542	$\begin{array}{c} -CHCH_2 \\ \\ NHCOOCH(CH_3)_2 \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
543	$\begin{array}{c} -CH \\ \\ OH \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
544	$\begin{array}{c} -CHCH_2 \\ \\ NHCOOC_2H_5 \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
545	$\begin{array}{c} -CHCH_2 \\ \\ NHSO_2CH_3 \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
546	$\begin{array}{c} -CH \\ \\ OH \\ \\ \text{Cyclohexyl ring} \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
547	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
548	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ OH	-H		1	C	Single bond
549	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H		1	C	—
550	$-\text{CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H		1	C	—
551	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array}$	-H		1	C	—
552	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ NHCOOC ₂ H ₅	-H		1	C	—
553	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ NHSO ₂ CH ₃	-H		1	C	—
554	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array}$	-H		1	C	—
555	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHCOOCH(CH ₃) ₂	-H		1	C	—
556	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ OH	-H		1	C	—

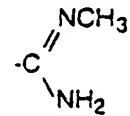
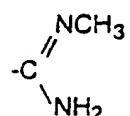
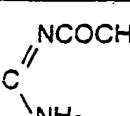
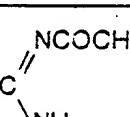
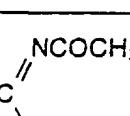
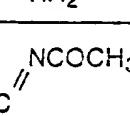
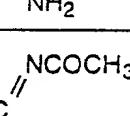
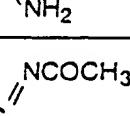
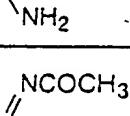
Table 1 (continued)

Compound No.	$-R^1 \left(-D-(CH)_{m-1}-E-R^4 \right)$	$-R^2$	$-R^3$	n	A	Broken line
557	$-CHCH_2-\begin{array}{c} H \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
558	$-CHCH_2-\begin{array}{c} H \\ \\ NHCOOC_2H_5 \end{array}$	+H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
559	$-CH-\begin{array}{c} H \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
560	$-CH-\begin{array}{c} H \\ \\ NHCOOC_2H_5 \end{array}$	+H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
561	$-CHCH_2C(CH_3)_3$ NHCOOC_2H_5	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
562	$-CHCH_2C(CH_3)_3$ NHCOOC(CH_3)_3	+H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
563	$-CHCH_2C(CH_3)_2$ OCOOC_2H_5	+H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
564	$-CHCH_2CH(CH_3)_2$ NHCOOCH(CH_3)_2	+H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
565	$-CHCH_2-\begin{array}{c} H \\ \\ NHCOOC(CH_3)_3 \end{array}$	+H	$\begin{array}{c} NCH_3 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
566	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
567	$\begin{array}{c} -CH- \text{C}_6\text{H}_4- \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
568	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
569	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
570	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
571	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	—
572	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	—
573	$\begin{array}{c} -CH- \text{C}_6\text{H}_4- \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	—
574	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ \parallel \\ -C \\ \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
575	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHCOC_2H_5	-H		1	C	—
576	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H		1	C	—
577	$-\text{CHCH}_2-\text{C}_6\text{H}_4-$ $\text{NHCOC}(\text{CH}_3)_3$	-H		1	C	Single bond
578	$-\text{CHCH}_2-\text{C}_6\text{H}_4-$ NHSO_2CH_3	-H		1	C	Single bond
579	$-\text{CH}-\text{C}_6\text{H}_4-$ OH	-H		1	C	Single bond
580	$-\text{CHCH}_2-\text{C}_6\text{H}_4-$ NHSO_2CH_3	-H		1	C	Single bond
581	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHCOC_2H_5	-H		1	C	Single bond
582	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H		1	C	Single bond
583	$-\text{CHCH}_2-\text{C}_6\text{H}_4-$ $\text{NHCOC}(\text{CH}_3)_3$	-H		1	C	—

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Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-} \text{R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
584	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NCOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
585	$\text{-CH} \text{-} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{-}$	-H	$\text{-C} \begin{array}{c} \text{NCOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
586	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NCOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
587	$\text{-CHCH}_2 \text{C(CH}_3)_3$ NHCOC_2H_5	-H	$\text{-C} \begin{array}{c} \text{NCOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
588	$\text{-CHCH}_2 \text{C(CH}_3)_3$ NHSO_2CH_3	-H	$\text{-C} \begin{array}{c} \text{NCOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
589	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHCOC(CH}_3)_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond
590	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond
591	$\text{-CH} \text{-} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{-}$	-H	$\text{-C} \begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond
592	$\text{-CHCH}_2 \text{-} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\text{-C} \begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
593	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
594	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
595	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
596	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
597	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
598	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
599	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
600	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
601	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(-D - (CH)_m - E - R^4 \right)$	$-R^2$	$-R^3$	n	A	Broken line
602	$-CHCH_2 - \begin{array}{c} H \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
603	$-CH - \begin{array}{c} H \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
604	$-CHCH_2 - \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
605	$-CHCH_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
606	$-CHCH_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
607	$-CHCH_2 - \begin{array}{c} H \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
608	$-CHCH_2 - \begin{array}{c} H \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
609	$-CH - \begin{array}{c} H \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
610	$-CHCH_2 - \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_3 \\ // \\ \text{C} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

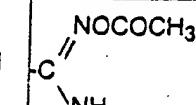
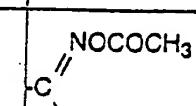
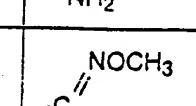
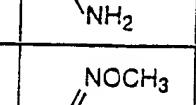
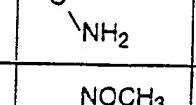
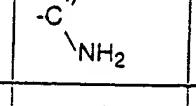
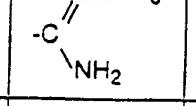
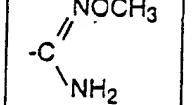
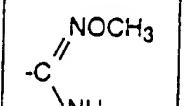
Compound No.	$-R_1 \left(-D-(CH)_m-E-R^4 \right)$	$-R_2$	$-R_3$	n	A	Broken line
611	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H		1	C	—
612	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H		1	C	—
613	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H		1	C	Single bond
614	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H		1	C	Single bond
615	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H		1	C	Single bond
616	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H		1	C	Single bond
617	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H		1	C	Single bond
618	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H		1	C	Single bond
619	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H		1	C	—

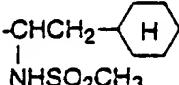
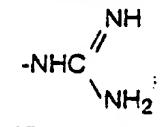
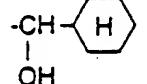
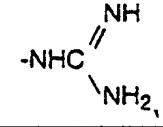
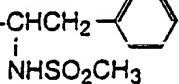
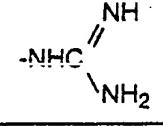
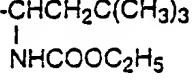
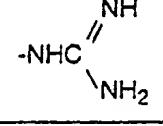
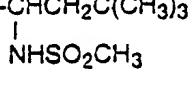
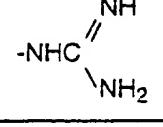
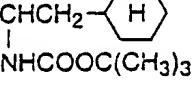
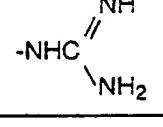
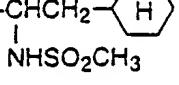
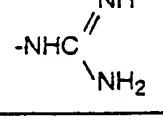
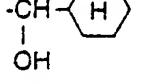
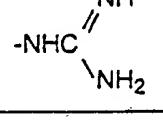
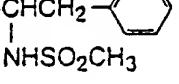
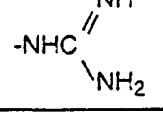
Table 1 (continued)

Compound No.	$-R^1 \left(-D-(CH)_m-E-R^4 \right)$	$-R^2$	$-R^3$	n	A	Broken line
620	$-CHCH_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
621	$-CH \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
622	$-CHCH_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
623	$-CHCH_2C(CH_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
624	$-CHCH_2C(CH_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
625	$-CHCH_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCCCH}_2\text{OH} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
626	$-CHCH_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
627	$-CH \begin{array}{c} \text{H} \\ \\ \text{OH} \end{math>$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
628	$-CHCH_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
629	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
630	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
631	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
632	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
633	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
634	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{C} \begin{array}{c} \text{NOCCCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
635	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
636	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{C} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
637	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R_5 \end{array} \right)$	$-R_2$	$-R_3$	n	A	Broken line
638		-H		1	C	Single bond
639		-H		1	C	Single bond
640		-H		1	C	Single bond
641		-H		1	C	Single bond
642		-H		1	C	Single bond
643		-H		1	C	—
644		-H		1	C	—
645		-H		1	C	—
646		-H		1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
647	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
648	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NH} \\ // \\ \text{NH}_2 \end{array}$	1	C	—
649	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
650	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
651	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
652	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
653	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
654	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	Single bond
655	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NCH}_3 \\ // \\ \text{NH}_2 \end{array}$	1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
656	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
657	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
658	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
659	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
660	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
661	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NCOCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
662	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCOCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
663	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NCOCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
664	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCOCH}_3 \\ // \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -O-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
665	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	Single bond
666	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	Single bond
667	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
668	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
669	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
670	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
671	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
672	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	—
673	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \diagup \\ \text{NOCOCH}_3 \\ \diagdown \end{array} \text{NH}_2$	1	C	Single bond

Table 1 (continued)

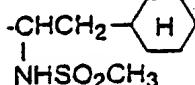
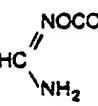
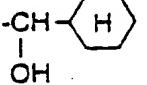
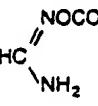
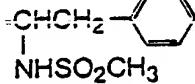
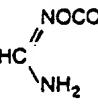
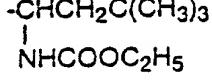
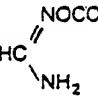
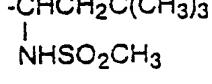
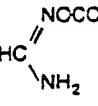
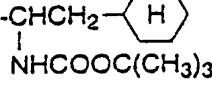
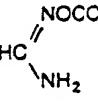
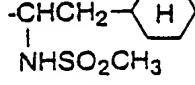
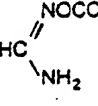
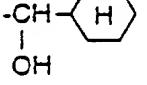
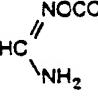
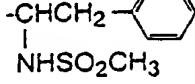
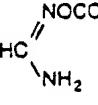
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
674		-H		1	C	Single bond
675		-H		1	C	Single bond
676		-H		1	C	Single bond
677		-H		1	C	Single bond
678		-H		1	C	Single bond
679		-H		1	C	—
680		-H		1	C	—
681		-H		1	C	—
682		-H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
683	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NOCOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	—
684	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NOCOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	—
685	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
686	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
687	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ OH \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
688	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
689	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
690	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
691	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NOCH_3 \\ \\ -NHC \\ \backslash \\ NH_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
692	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
693	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
694	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
695	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
696	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
697	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
698	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
699	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ \text{OH} \end{math>$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
700	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \diagup \\ \text{-NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
701	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
702	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond
703	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
704	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
705	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
706	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
707	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
708	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	—
709	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \parallel \\ \text{-NHC} \\ \backslash \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
710	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	Single bond
711	$-\text{CH}(\text{OH})-\text{C}_6\text{H}_4-\text{NH}_2$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	Single bond
712	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	Single bond
713	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $ \text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	Single bond
714	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $ \text{NHSO}_2\text{CH}_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	Single bond
715	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	—
716	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	—
717	$-\text{CH}(\text{OH})-\text{C}_6\text{H}_4-\text{NH}_2$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	—
718	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{NHSO}_2\text{CH}_3$	-H	$-\text{NHC}(=\text{O})\text{OCOCH}_3$ NH_2	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
719	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NOCOOCH}_3 \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	—
720	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOCOOCH}_3 \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	—
721	$-\text{CHCH}_2\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
722	$-\text{CHCH}_2\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
723	$-\text{CHC}_6\text{H}_5$ OH	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
724	$-\text{CHCH}_2\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
725	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
726	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	Single bond
727	$-\text{CHCH}_2\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NOH} \\ \text{ } \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(-D-(CH)_m-E-R^4 \right)$	$-R^2$	$-R^3$	n	A	Broken line
728	$-CHCH_2-\begin{array}{c} H \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
729	$-CH-\begin{array}{c} H \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
730	$-CHCH_2-\begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
731	$-CHCH_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
732	$-CHCH_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NOH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	—
733	$-CHCH_2-\begin{array}{c} H \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
734	$-CHCH_2-\begin{array}{c} H \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
735	$-CH-\begin{array}{c} H \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond
736	$-CHCH_2-\begin{array}{c} \text{H} \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	$\begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ -\text{NHC} \\ \diagdown \\ \text{NH}_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
737	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond
738	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	Single bond
739	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
740	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
741	$-\text{CH} \begin{array}{c} \text{C}_6\text{H}_5 \\ \\ \text{OH} \end{array}$	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
742	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
743	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
744	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NSO_2CH_3	-H	$-\text{NHC} \begin{array}{c} \text{NOCOCH}_2\text{OH} \\ \diagup \\ \text{NH}_2 \end{array}$	1	C	—
745	$-\text{CH} \begin{array}{c} \text{C}_6\text{H}_5 \\ \\ \text{NSO}_2\text{CH}_3 \end{array}$	-H	$-\text{NH}_2$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
746	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	-NH ₂	1	C	Single bond
747	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	-NH ₂	1	C	Single bond
748	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	H	-NH ₂	1	C	Single bond
749	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	H	-NH ₂	1	C	Single bond
750	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	H	-NH ₂	1	C	Single bond
751	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	-NH ₂	1	C	Single bond
752	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	-NH ₂	1	C	Single bond
753	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	H	-NH ₂	1	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R_4 \\ \\ R_5 \end{array} \right)$	-R2	-R3	n	A	Broken line
754	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	-NH ₂	1	C	Single bond
755	$\begin{array}{c} -CHCH_2- \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	1	C	Single bond
756	$\begin{array}{c} -CH- \\ \\ \text{OH} \end{array}$	-H	-NH ₂	1	C	Single bond
757	$\begin{array}{c} -CHCH_2\text{C(CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	1	C	Single bond
758	$\begin{array}{c} -CHCH_2\text{C(CH}_3)_3 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	-NH ₂	1	C	Single bond
759	$\begin{array}{c} -CH- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NH ₂	1	C	—
760	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NH ₂	1	C	—
761	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
762	$\begin{array}{c} -CH- \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	-NH ₂	1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
763	$-CHCH_2-\begin{array}{c} H \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	-NH ₂	1	C	—
764	$-CH-\begin{array}{c} H \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
765	$-CHCH_2-\begin{array}{c} H \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
766	$-CH-\begin{array}{c} H \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	-NH ₂	1	C	—
767	$-CH-\begin{array}{c} H \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
768	$-CH-\begin{array}{c} H \\ \\ OH \end{array}$	-H	-NH ₂	1	C	—
769	$-CH_2-\begin{array}{c} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
770	$-(CH_2)_3-\begin{array}{c} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
771	$-CH_2OCH_2-\begin{array}{c} \\ \\ \text{C}_6\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—

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Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-}(\text{CH})_m\text{-E-} \text{R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
772	$\text{-CH} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—
773	$\text{-CH}(\text{CH}_2)_2 \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—
774	$\text{-CHCH}_2\text{O} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOH}$	-H	-NH_2	1	C	—
775	$\text{-CHCH}_2\text{O} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_2 \begin{array}{c} \text{---} \\ \\ \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3 \end{array}$	-H	-NH_2	1	C	—
776	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—
777	$\text{-CH}_2\text{CH} \begin{array}{c} \text{---} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—
778	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NHCHO} \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—
779	$\text{-CHCH}_2 \begin{array}{c} \text{---} \\ \\ \text{NH}_2 \end{array} \text{---} \text{C}_6\text{H}_4 \text{---} \text{COOCH}_3$	-H	-NH_2	1	C	—

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
780	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
781	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	-NH ₂	1	C	—
782	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
783	$\begin{array}{c} -CH- \\ \\ OH \end{array}$	-H	-NH ₂	1	C	—
784	$\begin{array}{c} -CHCH_2- \\ \\ OCOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
785	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
786	$\begin{array}{c} -CHCH_2- \\ \\ OCONHCH_3 \end{array}$	-H	-NH ₂	1	C	—
787	$\begin{array}{c} -CHCH_2- \\ \\ OCONHCH_2CH=CH_2 \end{array}$	-H	-NH ₂	1	C	—
788	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—

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Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
789	$\begin{array}{c} -CH(CH_2)_2SCH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—
790	$\begin{array}{c} -CH(CH_2)_3CH_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—
791	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHSO_2CH_2COOH \end{array}$	-H	-NH ₂	1	C	—
792	$\begin{array}{c} -CH(CH_2)_2COOH \\ \\ NHSO_2-\text{C}_6\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
793	$\begin{array}{c} -CHC(SCH_3)(CH_3)_2 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
794	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
795	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
796	$\begin{array}{c} -CH(CH_2)_4CH_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
797	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	-NH ₂	1	C	—
798	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	-NH ₂	1	C	—

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
799	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
800	$\begin{array}{c} -CHCH_2CH(C_2H_5)_2 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
801	$\begin{array}{c} -CH(CH_2)_2SCH_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NH ₂	1	C	—
802	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH_2-\text{C}_6\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
803	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OH \end{array}$	-H	-NH ₂	1	C	—
804	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ OCOOC_2H_5 \end{array}$	-H	-NH ₂	1	C	—
805	$\begin{array}{c} -CHCH_2CH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—
806	$\begin{array}{c} -CHCH(CH_3)_2 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—
807	$\begin{array}{c} -CHC(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—
808	$\begin{array}{c} -CHCH_2SC(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NH ₂	1	C	—

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Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
809	$\text{-CHCH}_2 \text{OC(CH}_3)_3$ NHSO_2CH_3	-H	-NH ₂	1	C	—
810	$\text{-CHCH}_2 \text{OC(CH}_3)_2\text{C}_2\text{H}_5$ NHSO_2CH_3	-H	-NH ₂	1	C	—
811	$\text{-CHCH}_2 \text{O(C}_2\text{H}_5)_2\text{CH}_3$ NHSO_2CH_3	-H	-NH ₂	1	C	—
812	$\text{-CHC(CH}_3)_2\text{SCH}_3$ NHSO_2CH_3	-H	-NH ₂	1	C	—
813	$\text{-CHC(CH}_3)_2\text{SC}_2\text{H}_5$ NHSO_2CH_3	-H	-NH ₂	1	C	—
814	$\text{-CH} \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NH ₂	2	C	Single bond
815	$\text{-CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NH ₂	2	C	Single bond
816	$\text{-CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	Single bond
817	$\text{-CHCH}_2 \begin{array}{c} \text{H} \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	-NH ₂	2	C	Single bond

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R_4 \\ \\ R_5 \end{array} \right)$	-R2	-R3	n	A	Broken line
818	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	-NH ₂	2	C	Single bond
819	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ OH \end{array}$	-H	-NH ₂	2	C	Single bond
820	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NH ₂	2	C	Single bond
821	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	Single bond
822	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH(CH}_3)_2 \end{array}$	-H	-NH ₂	2	C	Single bond
823	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ \text{NHCOOC(CH}_3)_3 \end{array}$	-H	-NH ₂	2	C	Single bond
824	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ OCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	Single bond
825	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ OH \end{array}$	-H	-NH ₂	2	C	Single bond
826	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	Single bond

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Table 1 (continued)

Compound No.	$\text{-R}^1 \left(\begin{array}{c} \text{-D-(CH)}_m \text{-E-R}^4 \\ \\ \text{R}^5 \end{array} \right)$	-R^2	-R^3	n	A	Broken line
827	$\begin{array}{c} \text{-CHCH}_2 \text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	H	-NH ₂	2	C	Single bond
828	$\begin{array}{c} \text{-CH} \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	-NH ₂	2	C	—
829	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	-NH ₂	2	C	—
830	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	-NH ₂	2	C	—
831	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	H	-NH ₂	2	C	—
832	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	H	-NH ₂	2	C	—
833	$\begin{array}{c} \text{-CH} \text{---} \text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	H	-NH ₂	2	C	—
834	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	H	-NH ₂	2	C	—
835	$\begin{array}{c} \text{-CHCH}_2 \text{---} \text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	H	-NH ₂	2	C	—

Table 1 (continued)

Compound No.	$\cdot R^1 \left(\begin{array}{c} -O-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$\cdot R^2$	$\cdot R^3$	n	A	Broken line
836	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	-NH ₂	2	C	—
837	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-H	-NH ₂	2	C	—
838	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	—
839	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-H	-NH ₂	2	C	—
840	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	2	C	—
841	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	-NH ₂	2	C	—
842	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{NSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
843	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
844	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond

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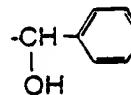
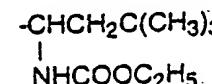
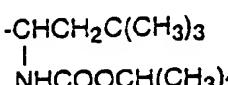
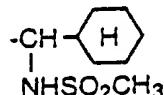
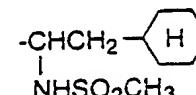
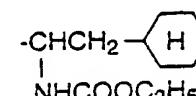
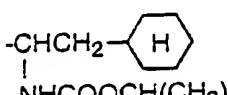
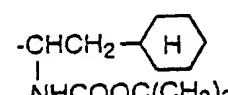
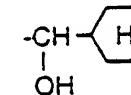
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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
845	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
846	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
847	$\begin{array}{c} -CH-\text{C}_6\text{H}_5 \\ \\ \text{OH} \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
848	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
849	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
850	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
851	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond
852	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
853		-CH ₃	-NH ₂	1	C	Single bond
854		-CH ₃	-NH ₂	1	C	Single bond
855		-CH ₃	-NH ₂	1	C	Single bond
856		-CH ₃	-NH ₂	1	C	—
857		-CH ₃	-NH ₂	1	C	—
858		-CH ₃	-NH ₂	1	C	—
859		-CH ₃	-NH ₂	1	C	—
860		-CH ₃	-NH ₂	1	C	—
861		-CH ₃	-NH ₂	1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
862	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	1	C	—
863	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	—
864	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	1	C	—
865	$\begin{array}{c} -CHCH_2- \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-CH ₃	-NH ₂	1	C	—
866	$\begin{array}{c} -CHCH_2- \\ \\ \text{OCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	—
867	$\begin{array}{c} -CH- \\ \\ \text{OH} \end{array}$	-CH ₃	-NH ₂	1	C	—
868	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	1	C	—
869	$\begin{array}{c} -CHCH_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	1	C	—
870	$\begin{array}{c} -CH- \\ \\ \text{H} \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ₂	-R ₃	n	A	Broken line
871	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
872	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
873	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
874	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_4 \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
875	$\begin{array}{c} -CH-\text{C}_6\text{H}_4 \\ \\ \text{OH} \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
876	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
877	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond
878	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-CH ₃	-NH ₂	2	C	Single bond

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	\AA	Broken line
879	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC(CH}_3)_3$	$-\text{CH}_3$	$-\text{NH}_2$	2	C	Single bond
880	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ OCOOC_2H_5	$-\text{CH}_3$	$-\text{NH}_2$	2	C	Single bond
881	$-\text{CH}-\text{C}_6\text{H}_5$ OH	$-\text{CH}_3$	$-\text{NH}_2$	2	C	Single bond
882	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	$-\text{CH}_3$	$-\text{NH}_2$	2	C	Single bond
883	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOCH}(\text{CH}_3)_2$	$-\text{CH}_3$	$-\text{NH}_2$	2	C	Single bond
884	$-\text{CH}-\text{C}_6\text{H}_5$ NHSO_2CH_3	$-\text{CH}_3$	$-\text{NH}_2$	2	C	—
885	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	$-\text{CH}_3$	$-\text{NH}_2$	2	C	—
886	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}_2\text{H}_5$	$-\text{CH}_3$	$-\text{NH}_2$	2	C	—
887	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOCH}(\text{CH}_3)_2$	$-\text{CH}_3$	$-\text{NH}_2$	2	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
888	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC(CH_3)_3 \end{array}$	-CH ₃	-NH ₂	2	C	—
889	$\begin{array}{c} -CH- \\ \\ OH \end{array}$	-CH ₃	-NH ₂	2	C	—
890	$\begin{array}{c} -CHCH_2- \\ \\ NHSO_2CH_3 \end{array}$	-CH ₃	-NH ₂	2	C	—
891	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC_2H_5 \end{array}$	-CH ₃	-NH ₂	2	C	—
892	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-CH ₃	-NH ₂	2	C	—
893	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOC(CH_3)_3 \end{array}$	-CH ₃	-NH ₂	2	C	—
894	$\begin{array}{c} -CHCH_2- \\ \\ OCOOC_2H_5 \end{array}$	-CH ₃	-NH ₂	2	C	—
895	$\begin{array}{c} -CH- \\ \\ OH \end{array}$	-CH ₃	-NH ₂	2	C	—
896	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-CH ₃	-NH ₂	2	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
897	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-CH ₃	-NH ₂	2	C	—
898	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NHCH ₃	1	C	Single bond
899	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCH ₃	1	C	Single bond
900	$\begin{array}{c} -CH-\text{C}_6\text{H}_5 \\ \\ OH \end{array}$	-H	-NHCH ₃	1	C	Single bond
901	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCH ₃	1	C	Single bond
902	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NHCH ₃	1	C	Single bond
903	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCH ₃	1	C	Single bond
904	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NHCH ₃	1	C	—
905	$\begin{array}{c} -CHCH_2-\text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCH ₃	1	C	—

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Table 1 (continued)

Compound No.	$-R_1 \left(-O-(CH)_m-E-R^4 \right)$	$-R_2$	$-R_3$	n	A	Broken line
906	$-CH \begin{cases} H \\ \\ OH \end{cases} - \text{C}_6\text{H}_5$	-H	-NHCH ₃	1	C	—
907	$-CHCH_2 \begin{cases} H \\ \\ \text{NSO}_2\text{CH}_3 \end{cases} - \text{C}_6\text{H}_5$	-H	-NHCH ₃	1	C	—
908	$-CHCH_2 \begin{cases} C(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{cases}$	-H	-NHCH ₃	1	C	—
909	$-CHCH_2 \begin{cases} C(\text{CH}_3)_3 \\ \\ \text{NSO}_2\text{CH}_3 \end{cases}$	-H	-NHCH ₃	1	C	—
910	$-CHCH_2 \begin{cases} H \\ \\ \text{NHCOOC}(\text{CH}_3)_3 \end{cases} - \text{C}_6\text{H}_5$	-H	-NHC ₂ H ₅	1	C	Single bond
911	$-CHCH_2 \begin{cases} H \\ \\ \text{NSO}_2\text{CH}_3 \end{cases} - \text{C}_6\text{H}_5$	-H	-NHC ₂ H ₅	1	C	Single bond
912	$-CH \begin{cases} H \\ \\ OH \end{cases} - \text{C}_6\text{H}_5$	-H	-NHC ₂ H ₅	1	C	Single bond
913	$-CHCH_2 \begin{cases} H \\ \\ \text{NSO}_2\text{CH}_3 \end{cases} - \text{C}_6\text{H}_5$	-H	-NHC ₂ H ₅	1	C	Single bond
914	$-CHCH_2 \begin{cases} C(\text{CH}_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{cases}$	-H	-NHC ₂ H ₅	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH_m-E-R^4) \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
915	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHC ₂ H ₅	1	C	Single bond
916	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NHC ₂ H ₅	1	C	—
917	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHC ₂ H ₅	1	C	—
918	$\begin{array}{c} -CH \text{---} \text{C}_6\text{H}_5 \\ \\ OH \end{array}$	-H	-NHC ₂ H ₅	1	C	—
919	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHC ₂ H ₅	1	C	—
920	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NHC ₂ H ₅	1	C	—
921	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHC ₂ H ₅	1	C	—
922	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NHCOCH ₃	1	C	Single bond
923	$\begin{array}{c} -CHCH_2 \text{---} \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOCH ₃	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	$-R^2$	$-R^3$	n	A	Broken line
924	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ OH \end{array}$	-H	-NHCOCH ₃	1	C	Single bond
925	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOCH ₃	1	C	Single bond
926	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NHCOCH ₃	1	C	Single bond
927	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOCH ₃	1	C	Single bond
928	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ NHCOOC(CH3)3 \end{array}$	-H	-NHCOCH ₃	1	C	—
929	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOCH ₃	1	C	—
930	$\begin{array}{c} -CH- \text{C}_6\text{H}_4 \\ \\ OH \end{array}$	-H	-NHCOCH ₃	1	C	—
931	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_4 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOCH ₃	1	C	—
932	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NHCOCH ₃	1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
933	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	-NHCOCH ₃	1	C	—
934	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	-NHCOOCH ₃	1	C	Single bond
935	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	-NHCOOCH ₃	1	C	Single bond
936	$-\text{CH}-\text{C}_6\text{H}_5$ OH	-H	-NHCOOCH ₃	1	C	Single bond
937	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	-NHCOOCH ₃	1	C	Single bond
938	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H	-NHCOOCH ₃	1	C	Single bond
939	$-\text{CHCH}_2\text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H	-NHCOOCH ₃	1	C	Single bond
940	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H	-NHCOOCH ₃	1	C	—
941	$-\text{CHCH}_2-\text{C}_6\text{H}_5$ NHSO_2CH_3	-H	-NHCOOCH ₃	1	C	—

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
942	$-CH \begin{array}{c} H \\ \\ OH \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOCH ₃	1	C	—
943	$-CHCH_2 \begin{array}{c} H \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOCH ₃	1	C	—
944	$-CHCH_2 \begin{array}{c} C(CH_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NHCOOCH ₃	1	C	—
945	$-CHCH_2 \begin{array}{c} C(CH_3)_3 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array}$	-H	-NHCOOCH ₃	1	C	—
946	$-CHCH_2 \begin{array}{c} H \\ \\ \text{NHCOOC(CH}_3)_3 \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond
947	$-CHCH_2 \begin{array}{c} H \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond
948	$-CH \begin{array}{c} H \\ \\ OH \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond
949	$-CHCH_2 \begin{array}{c} H \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{---} \text{C}_6\text{H}_5$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond
950	$-CHCH_2 \begin{array}{c} C(CH_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond

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Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R ²	-R ³	n	A	Broken line
951	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	Single bond
952	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
953	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
954	$\begin{array}{c} -CH- \text{C}_6\text{H}_5 \\ \\ OH \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
955	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
956	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
957	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	-NHCOOC(CH ₃) ₃	1	C	—
958	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} \text{CH}_3 \\ \\ -\text{NHCH}_2-\text{C}(=\text{O})-\text{O}-\text{C}(=\text{O})-\text{O} \end{array}$	1	C	Single bond
959	$\begin{array}{c} -CHCH_2- \text{C}_6\text{H}_5 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{CH}_3 \\ \\ -\text{NHCH}_2-\text{C}(=\text{O})-\text{O}-\text{C}(=\text{O})-\text{O} \end{array}$	1	C	Single bond

Table 1 (continued)

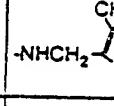
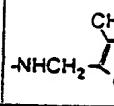
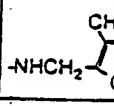
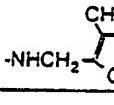
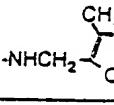
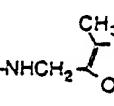
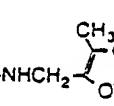
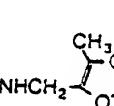
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
960	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{C}_6\text{H}_5$	-H		1	C	Single bond
961	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ NHSO_2CH_3	-H		1	C	Single bond
962	$-\text{CHCH}_2 \text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H		1	C	Single bond
963	$-\text{CHCH}_2 \text{C}(\text{CH}_3)_3$ NHSO_2CH_3	-H		1	C	Single bond
964	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ $\text{NHCOOC}(\text{CH}_3)_3$	-H		1	C	—
965	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ NHSO_2CH_3	-H		1	C	—
966	$-\text{CH} \begin{array}{c} \text{H} \\ \\ \text{OH} \end{array} \text{C}_6\text{H}_5$	-H		1	C	—
967	$-\text{CHCH}_2 \text{C}_6\text{H}_5$ NHSO_2CH_3	-H		1	C	—

Table 1 (continued)

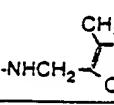
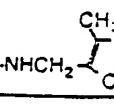
Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
968	$-\text{CHCH}_2 \text{C}(\text{CH}_3)_3$ $\text{NHCOOC}_2\text{H}_5$	-H		1	C	—
969	$-\text{CHCH}_2 \text{C}(\text{CH}_3)_3$ $\text{NHSO}_2\text{C}_2\text{H}_5$	-H		1	C	—

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
970	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_4-\text{COOH}$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
971	$-\text{CHCH}_2-\text{C}_6\text{H}_4-\text{OCH}_2\text{COOC}_2\text{H}_5$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
972	$-\text{CHCH}_2-\text{C}_6\text{H}_4-$ NHCOC_2H_5	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
973	$-\text{CH}(\text{CH}_2)_4\text{CH}_3$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
974	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_4-$ NHSO_2CH_3 CH_2COOH	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
975	$-\text{CHCH}_2\text{O}-\text{C}_6\text{H}_4-\text{CH}_2\text{COOH}$ NHSO_2CH_3	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
976	$-\text{CH}(\text{CH}_2)_4\text{CH}_3$ $\text{NHSO}_2\text{CH}_2\text{COOC}_2\text{H}_5$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	Single bond
977	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ $\text{NHCOC}(\text{CH}_3)_2$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
978	$-\text{CHCH}_2\text{OC}(\text{CH}_3)_2\text{C}_2\text{H}_5$ NHCOC_2H_5	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—
979	$-\text{CHCH}_2\text{OC}(\text{C}_2\text{H}_5)_2\text{CH}_3$ $\text{NHCOC}(\text{CH}_3)_2$	-H	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C} \\ \\ \text{NH}_2 \end{array}$	1	C	—

Table 1 (continued)

Compound No.	$-R_1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R_5 \end{array} \right)$	-R2	-R3	n	A	Broken line
980	$\begin{array}{c} -CHCH_2SC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	—
981	$\begin{array}{c} CH_3 \\ \\ -CHCH_2O \\ \\ NHCOOCH(CH_3)_2 \end{array}$	H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	—
982	$\begin{array}{c} -CHCH(CH_3)OC(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	—
983	$\begin{array}{c} -CHC(CH_3)_2SCH(CH_3)_2 \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	—
984	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH_2COOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond
985	$\begin{array}{c} -CH- \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond
986	$\begin{array}{c} -CH- \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond
987	$\begin{array}{c} -CH- \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond
988	$\begin{array}{c} -CHCH_2- \\ \\ NHCOOCH_2- \\ \\ NHCOOC_2H_5 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond
989	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHCOOC(CH_3)_3 \end{array}$	H	$\begin{array}{c} NOH \\ \\ -C \\ \backslash \quad / \\ NH_2 \end{array}$	1	C	Single bond

Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
990	$\begin{array}{c} -CHCH_2- \\ \\ NHCON(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
991	$\begin{array}{c} -CHCH_2COOC(CH_3)_3 \\ \\ NHCOOCH_2- \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	Single bond
992	$\begin{array}{c} -CHCH_2OH \\ \\ NHCOOC(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
993	$\begin{array}{c} -CHCH(CH_3)OC(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
994	$\begin{array}{c} -CH- \\ \\ OCOCH_3 \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
995	$\begin{array}{c} CH_3 \\ \\ -CHCH_2O- \\ \\ NHCOOCH(CH_3)_3 \end{array}$	-H	$\begin{array}{c} NOH \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
996	$\begin{array}{c} -CHCH_2OC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NOCOOCH_3 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
997	$\begin{array}{c} -CHCH_2CH(CH_3)_2 \\ \\ OH \end{array}$	-H	$\begin{array}{c} NOCOOC_2H_5 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
998	$\begin{array}{c} -CHCH_2OC(CH_3)_3 \\ \\ NHCOOC_2H_5 \end{array}$	-H	$\begin{array}{c} NOCOOCH_3 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—
999	$\begin{array}{c} -CHCH_2OC(CH_3)_3 \\ \\ NHCOOCH(CH_3)_2 \end{array}$	-H	$\begin{array}{c} NOCOOCH_3 \\ // \\ -C \\ \backslash \\ NH_2 \end{array}$	1	C	—

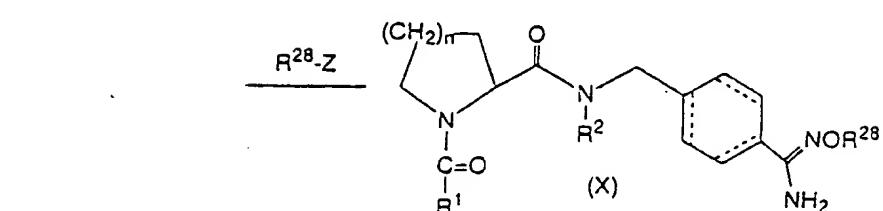
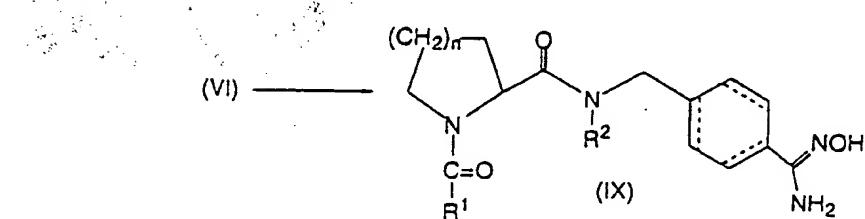
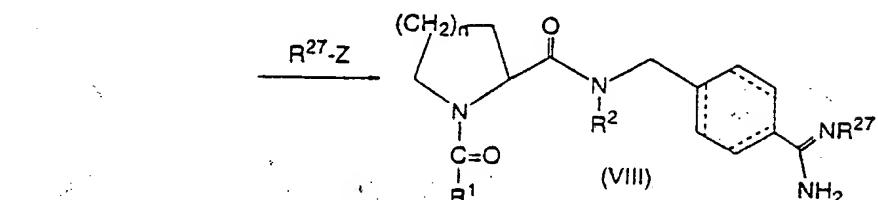
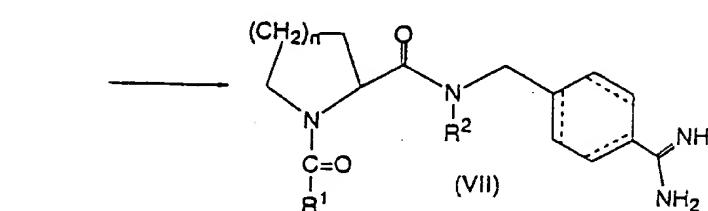
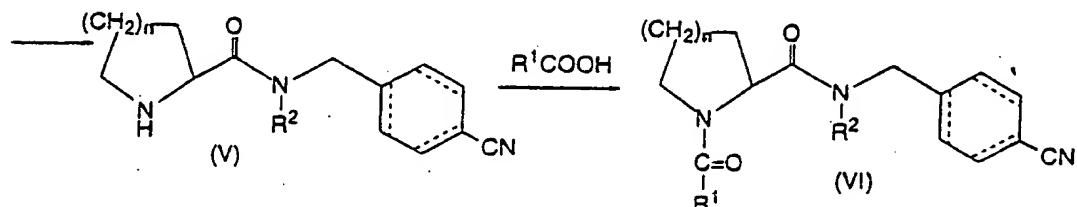
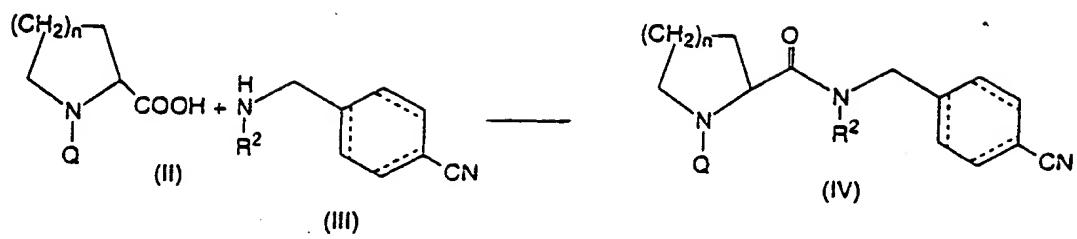
Table 1 (continued)

Compound No.	$-R^1 \left(\begin{array}{c} -D-(CH)_m-E-R^4 \\ \\ R^5 \end{array} \right)$	-R2	-R3	n	A	Broken line
1000	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ NHSO_2CH_3 \end{array}$	-H	$\begin{array}{c} \text{NCOOC}_2\text{H}_5 \\ \text{C}=\text{NH}_2 \end{array}$	1	C	Single bond
1001	$\begin{array}{c} -CH \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{NCOOCH}_3 \\ \text{C}=\text{NH}_2 \end{array}$	1	C	Single bond
1002	$\begin{array}{c} -CHCH_2 \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{C}_6\text{H}_4\text{OCH}_3$	-H	-NH ₂	1	C	—
1003	$\begin{array}{c} -CHCH_2OC(CH_3)_3 \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array}$	-H	-NH ₂	1	C	—
1004	$\begin{array}{c} -CH \\ \\ \text{NHCOOC}_2\text{H}_5 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{CH}_3 \\ \text{O} \\ \text{NHCH}_2-\text{C}(=\text{O})-\text{C}(=\text{O})-\text{O} \end{array}$	1	C	—
1005	$\begin{array}{c} -CHCH_2C(CH_3)_3 \\ \\ \text{NHCOOCH}(\text{CH}_3)_2 \end{array}$	-H	$\begin{array}{c} \text{CH}_3 \\ \text{O} \\ \text{NHCH}_2-\text{C}(=\text{O})-\text{C}(=\text{O})-\text{O} \end{array}$	1	C	—
1006	$\begin{array}{c} -CH \\ \\ \text{NHSO}_2\text{CH}_3 \end{array} \text{C}_6\text{H}_5$	-H	$\begin{array}{c} \text{CH}_3 \\ \text{O} \\ \text{NHCH}_2-\text{C}(=\text{O})-\text{C}(=\text{O})-\text{O} \end{array}$	1	C	—

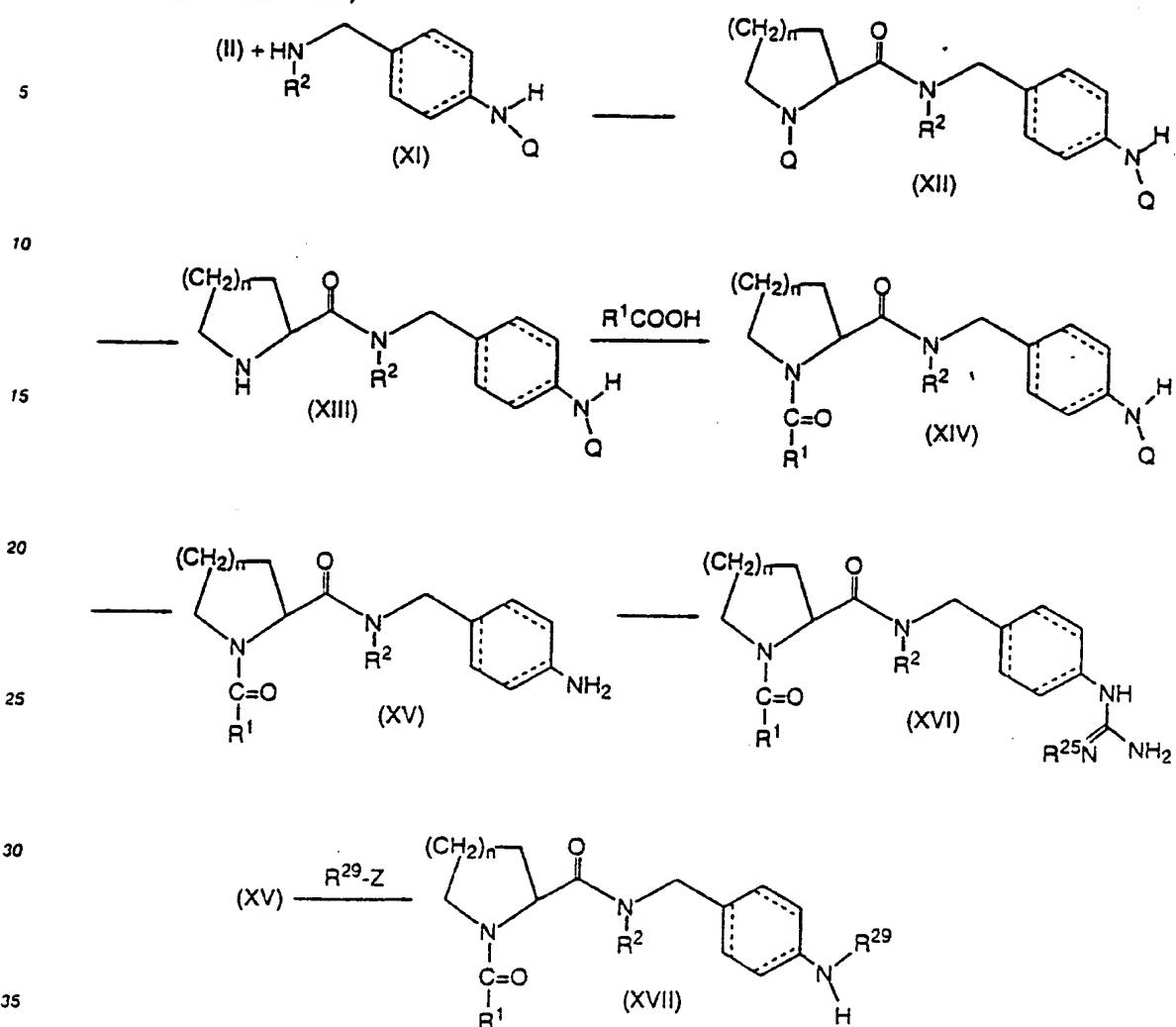
Hereinafter, the production process for the compounds of the present invention will be explained.

The compounds of the present invention can be produced through any combination of reactions suitable for the objective compounds. Typical reaction schemes will be shown below, but they should not be construed to be limiting the scope of the present invention.

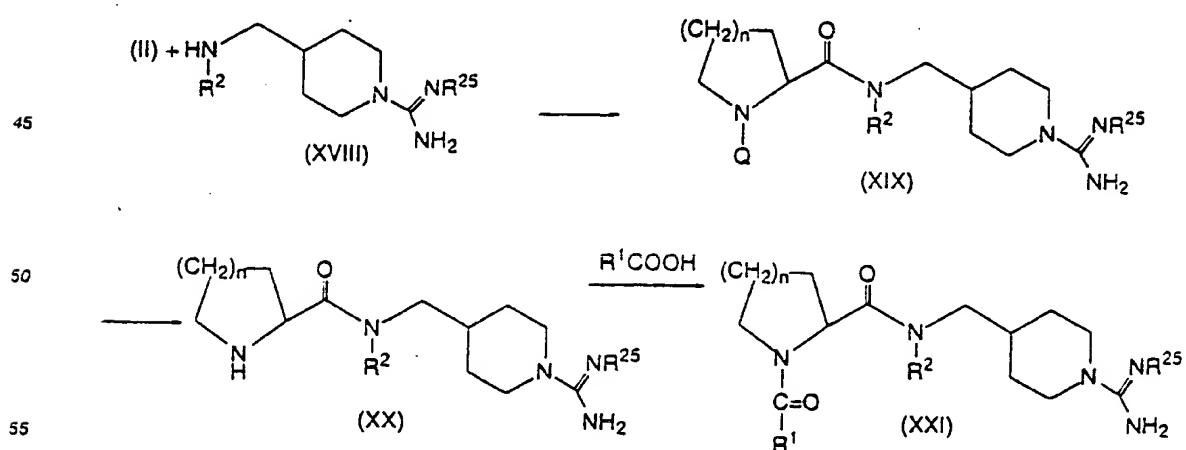
(Reaction scheme I)



(Reaction scheme II)



(Reaction scheme III)



wherein R¹, R², R²⁵, n and broken line are as defined above; Q is an amino-protecting group, such as benzyloxycarbonyl group, tertiary butyloxycarbonyl group, etc.; Z is a leaving group such as halogen atom, methanesulfonyloxy group, toluenesulfonyloxy group, trifluoromethylsulfonyloxy group, acetoxy (acetyloxy) group, etc.; R²⁷, R²⁸ and R²⁹ indicate a specific substituent contained in R²⁵ and R²⁶; R²⁷ is a C₁-C₆ alkyl group, a C₂-C₇ acyl group or a C₂-C₇ alkoxycarbonyl group; R²⁸ is a C₁-C₆ alkyl group, a C₂-C₇ acyl group, a C₂-C₇ alkoxycarbonyl group or a C₂-C₇ hydroxyalkylcarbonyl group; R²⁹ is a C₁-C₆ alkyl group, a C₂-C₇ acyl group, a C₂-C₇ alkoxycarbonyl group or 5-C₁-C₃ alkyl-1,3-dioxol-2-on-4-ylmethyl group.

In the above reaction schemes, a known method for synthesizing amide can be used for synthesizing the compounds (IV), (VI), (XII), (XIV), (XIX) and (XXI). There are various conventional methods, for example, a method using dehydrating agents such as dicyclohexylcarbodiimide, 1-ethyl-3-(dimethylaminopropyl)-carbodiimide, carbonyldiimidazole, etc., azido method, acid halide method, acid anhydride method, active ester method and the like. (e.g., see, "JIKKEN KAGAKU KOZA, 22, YUKI-GOSEI IV", pp. 259 - (1992), ed. "JAPAN Chemical Society", 4th. edition, published by Maruzen). The reaction is conducted under cooling or heating (or at room temperature) using an inert solvent such as tetrahydrofuran, diethyl ether, dichloromethane, etc. in a conventional manner. In the above schemes, the compounds (V), (XIII), (XV) and (XX) can be synthesized by deprotection according to a method known in the peptide chemistry (e.g. see "The Principle and Experimental Procedures of Peptide Synthesis" written by Nobuo IZUMIYA et al., published by Maruzen).

Further, the compound (VII) is synthesized by reacting imidate, which is obtained by reacting the compound (VI) with alcohol and an inorganic acid such as hydrochloric acid, with ammonia or an ammonium salt; or by reacting a thioamide compound, which is obtained by reacting the compound (VI) with hydrogen sulfide in the presence of an organic base such as triethylamine, pyridine, etc., with a lower alkylhalogen compound such as methyl iodide, etc., followed by reacting the resulting thioimidate compound with ammonia or an ammonium salt. Further, the compound (IX) is synthesized by reacting the compound (VI) with hydroxylamine or acid adduct thereof in a suitable solvent such as water, alcohol, tetrahydrofuran, etc. at room temperature or under heating.

Further, the compounds (VIII), (X) and (XVI) are synthesized by reacting the compounds (VII), (IX) and (XV) with R²⁷-Z, R²⁸-Z or R²⁹-Z in an inert solvent such as tetrahydrofuran, ether, dichloromethane, etc. in the presence of an organic or inorganic base under cooling or heating (or at room temperature), respectively.

Further, the compound (XVI) is synthesized by reacting the compound (XV) with a guanidizing reagent such as 2-alkylisothiourea derivative or acid adduct thereof in a suitable solvent such as water, alcohol, tetrahydrofuran, etc. at room temperature or under heating.

The respective compounds thus obtained can be isolated and purified by conventional chemical procedures such as extraction, crystallization, recrystallization, various chromatography and the like.

When the compounds of the present invention are used for clinical application, a proportion of a therapeutically active ingredient to a carrier component varies within a range of 1 to 90% by weight. For example, the compounds of the present invention may be orally administered in the dosage form such as granules, fine granules, powders, tablets, hard capsules, soft capsules, syrups, emulsions, suspensions, solutions and the like, or intravenously, intramuscularly or subcutaneously administered in the form of injections. Further, they may also be used in the form of suppositories. They may also be formed into powders which can be converted into solutions or the like for injection before use. There can be used pharmaceutical organic or inorganic solid or liquid carriers or diluents which are suitable for oral, intestinal or parenteral administration for preparing the drugs of the present invention. As the excipient used for preparing solid preparations, for example, there can be used lactose, sucrose, starch, talc, cellulose, dextrin, kaoline, calcium carbonate and the like. Liquid preparations for oral administration, i.e. emulsions, syrups, suspensions, solutions, etc. contain inert diluents which are normally used, e.g. water, vegetable oil, etc. This preparation can contain adjuvants such as humectants, suspension auxiliary agents, sweeteners, aromatics, colorants, preservatives, etc., in addition to inert diluents. The resulting liquid preparations may be contained in a capsule of an absorbable substance such as gelatin. As the solvent or suspending agent used for preparing preparations for parenteral administration, i.e. injections, suppositories, etc., for example, there can be used water, propylene glycol, polyethylene glycol, benzyl alcohol, ethyl oleate, lecithin and the like. As the base used for preparing suppositories, for example, there can be used cacao butter, emulsified cacao butter, laurin tallow, witepsol and the like. Preparations may be prepared by a conventional method.

The clinical dose varies depending upon age, pathology, condition of diseases and the like. For example, in the case of administering orally to an adult patient, the compounds of the present invention are normally administered with a dairy dose of about 0.01 to 1000 mg, preferably 10 to 1000 mg. The pharmaceutical composition of the present invention may be administered 1 to 3 times per day or

administered intermittently with the above dairy dose.

When using as injections, it is advantageous that the compounds of the present invention are administered continuously or intermittently to an adult patient with a single dose of 0.001 to 100 mg.

The prolineamide derivatives of the present invention or the salts thereof have a strong inhibition activity 5 to proteases such as thrombin, trypsin and the like. The compounds of the present invention are also superior in oral absorptive action so that they are useful as oral antithrombin agents, i.e. oral anticoagulants, or oral antitrypsin agents, i.e. remedy for pancreas diseases such as pancreatitis.

The following Examples and Experimental Examples further illustrate the present invention in detail but are not to be construed to limit the scope thereof.

10 The conventional abbreviations used in Examples are as follows: THF: tetrahydrofuran, DMF: N,N-dimethylformamide, DMSO: dimethyl sulfoxide, CDI: carbonyldiimidazole, DPPA: diphenylphosphorylazide, Z: benzyloxycarbonyl, Boc: tertiary butyloxycarbonyl.

15 Further, NMR in physical properties stands for a nuclear magnetic resonance spectrum and the numeral is δ value in ppm, which is conventionally used for indicating the chemical shift. TMS (tetramethylsilane) was used as the internal standard. Further, the numeral shown in parenthesis following δ value is the number of hydrogen atoms, and the indications following the number of hydrogen atoms mean that s is singlet, d is doublet, t is triplet, q is quartet, m is multiplet, br is broad absorption peak, respectively.

20 IR stands for an infrared spectrum and measured as potassium bromide tablets unless otherwise stated. The numerical means the wave number in cm^{-1} . Only main absorption peak was shown. Further, mp means the non-corrected melting point in $^{\circ}\text{C}$.

Example 1

25 Synthesis of 4-amidino-[(S)-N-((R)-2-methylsulfonylaminocyclohexylacetyl) proyl]aminomethylbenzene (compound No. 105 of Table 1) hydrochloride

(a) N-4-cyanobenzylphthalimide

30 To a solution of potassium phthalimide (76 g, 410 mmol) in DMF (250 ml), a solution of 4-cyanobenzyl bromide (73 g, 373 mmol) in THF (250 ml) is added and stirred at 50°C for 3 hours.

Water (500 ml) is added to the mixture and a precipitated crystal was collected. Then, the crystal is washed with water and dried to give 96 g of the titled compound (99%). mp: 189-191 $^{\circ}\text{C}$.

(b) 4-Cyano-[(S)-prolyl]aminomethylbenzene hydrochloride

35 To a solution of the compound (39 g, 150 mmol) obtained in the item (a) in methanol (250 ml), hydrazine hydrate (9 ml) is added and refluxed for 6 hours. After the solvent is evaporated, an aqueous 40% sodium hydroxide solution (300 ml) is added to the residue and stirred.

40 The reaction mixture is extracted with toluene and the organic layer is washed once with water and saturated brine, successively, and then dried over sodium sulfate. The solvent is evaporated and the resulting crude product (15 g, 73%) is used for the next step.

To a solution of (S)-N-Boc-proline (23.7 g, 110 mmol) in THF (250 ml), CDI (17.8 g, 110 mmol) is added at 0°C .

45 After the reaction solution is stirred for 2 hours, a solution of the crude product obtained in the above reaction in THF (150 ml) is added. After stirring for 6 hours, the solvent is evaporated and water (300 ml) is added to the residue. The mixture is extracted with chloroform and the organic layer is washed three times with water and once with saturated brine, successively. After drying over sodium sulfate, the solvent is evaporated and the residue is purified with silica gel chromatography (hexane-ethyl acetate).

The resulting oily product is dissolved in ethyl acetate (100 ml) and a 4N-hydrochloride in ethyl acetate 50 (69 ml) is added and the mixture is stirred at 0°C for 3 hours. The precipitated white solid is collected, washed with ethyl acetate and dried under reduced pressure to give 25.9 g of the titled compound (89%).

NMR (DMSO- d_6)

55 1.80-1.96 (m, 3H), 2.30-2.40 (m, 1H), 3.21 (br, 2H), 4.26 (br, 1H), 4.44 (d, 2H), 7.49 (d, 2H), 7.82 (d, 2H), 8.59 (br, 1H), 9.39 (t, 1H), 10.07 (br, 1H)

(c) 4-Cyano-[(S)-N-((R)-2-t-butyloxycarbonylamino-cyclohexylacetyl) prolyl]aminomethylbenzene

To a solution of the product (21 g, 79 mmol) obtained in the item (b) and (R)-N-t-butyloxycarbonyl-cyclohexylglycine (20.4 g, 79 mmol) in DMF (200 ml), a solution of triethylamine (22 ml, 159 mmol) and DPPA (22 g, 79 mmol) in DMF (50 ml) is added at 0 °C. The mixture is allowed to stand at room temperature and then stirred for 12 hours. Water (400 ml) is added to the reaction mixture which is extracted with toluene-ethyl acetate (1:2). The organic layer is washed three times with water and once with saturated brine, successively, and then dried over sodium sulfate. After the solvent is evaporated, the residue is purified with silica gel chromatography (chloroform-methanol) to give 26.7 g of the titled compound (72%).

NMR (CDCl₃)

1.01-1.43 (m, 15H), 1.65-2.38 (m, 9H), 3.57 (q, 1H), 3.96-4.06 (m, 2H), 4.47 (dq, 2H), 4.69 (d, 1H), 5.12 (d, 1H), 7.35 (d, 2H), 7.59 (d, 2H), 7.73 (t, 1H)

5 (d) 4-Cyano-[(S)-N-((R)-2-methylsulfonylamino-cyclohexylacetyl)prolyl] aminomethylbenzene

To a solution of the compound (26.7 g, 57 mmol) obtained in the item (c) in chloroform (50 ml), a 4-N hydrochloride in ethyl acetate (30 ml) is added at 0 °C. The mixture is stirred for 3 hours and then the solvent is evaporated. The resulting residue was dissolved in dichloromethane (250 ml) and triethylamine (19 ml) is added. Then, a solution of methanesulfonyl chloride (7.9 g, 68 mmol) in dichloromethane (50 ml) is added at 0 °C and the mixture is stirred for 3 hours. The organic layer is washed once with a saturated sodium bicarbonate solution, water and saturated brine, successively, and then dried over sodium sulfate. The resulting residue is purified with silica gel chromatography (hexane-ethyl acetate) to give 18.6 g of the titled compound (73%).

6 NMR (CDCl₃)

0.9-1.29 (m, 5H), 1.60-1.85 (m, 5H), 2.0-2.4 (m, 5H), 2.89 (s, 3H), 3.55 (q, 1H), 3.80-3.88 (m, 2H), 4.43 (d, 2H), 4.61 (d, 2H), 5.60 (d, 2H), 7.31 (t, 1H), 7.37 (d, 2H), 7.60 (d, 2H)

(e) 4-Amidino-[(S)-N-((R)-2-methylsulfonylamino-cyclohexylacetyl) prolyl]aminomethylbenzene chloride

To a solution of the compound (18.6 g, 42 mmol) obtained in the item (d) in chloroform (100 ml), a 37% hydrochloride in ethanol (100 ml) is added at 0 °C. The mixture is allowed to stand at 0 °C for 48 hours and then the solvent is evaporated. The resulting residue is dissolved in methanol (100 ml) and ammonium carbonate (16 g, 166 mmol) is added at 0 °C. After stirring for 6 hours, the solvent is evaporated and the resulting residue is purified with silica gel chromatography (chloroform-methanol) to give 5.2 g of the titled compound (73%).

NMR (DMSO-d₆)

9.39 (br, 4H), 8.66 (t, 1H), 7.81 (d, 2H), 7.48 (d, 2H), 7.40 (m, 1H), 4.47-4.14 (m, 3H), 3.90 (m, 1H), 3.71 (m, 1H), 3.59 (m, 1H), 2.79 (s, 3H), 2.13 (m, 1H), 1.88 (m, 3H), 1.69-1.53 (m, 5H), 1.14 (m, 6H)

7 IR: 3366, 2930, 2855, 1636, 1541, 1489, 1451, 1152

According to the same procedures described above, the compounds shown in the following Examples were synthesized.

Example 2

5 4-Amidino-[(S)-N-[(R)-2-methylsulfonylamino-4,4-dimethylpentanoyl] prolyl]aminomethylbenzene (compound No. 104 of Table 1) methanesulfonate

NMR (DMSO-d₆)

9.31 (br, 2H), 9.11 (br, 2H), 8.60 (t, 1H), 7.76 (d, 2H), 7.47 (d, 2H), 7.42 (d, 2H), 4.50-4.06 (m, 4H), 3.49 (m, 1H), 3.71 (m, 1H), 2.71 (s, 3H), 2.40 (s, 3H), 2.13 (m, 1H), 1.98 (m, 2H), 1.84 (m, 1H), 1.48 (d, 2H), 0.98 (s, 9H)

IR: 3274, 2957, 1640, 1208, 1150, 1049

Example 3

4-Amidino-[(S)-N [(R)-2-methylsulfonylamino-3-cyclohexylpropionyl] prolyl]aminomethylbenzene (compound No. 106 of Table 1) hydrochloride

5 NMR (DMSO-d₆)
 9.41 (br, 2H), 9.20 (br, 2H), 8.68 (t, 1H), 7.78 (d, 2H), 7.47 (d, 2H), 7.41 (d, 2H), 4.49-4.23 (m, 3H), 4.13
 (m, 1H), 3.69 (m, 1H), 3.48 (m, 1H), 2.72 (s, 3H), 2.12 (m, 1H), 1.97 (m, 1H), 1.83 (m, 2H), 1.64 (m, 5H),
 1.40 (m, 2H), 1.19 (m, 4H), 0.94 (m, 2H)

10 IR: 3366, 2924, 1640, 1543, 1489, 1449, 1422

Example 4

4-Amidino-[(S)-N [(R)-N'-methylsulfonylphenylalanyl] prolyl] aminomethylbenzene (compound No. 108 of Table 1) methanesulfonate

NMR (DMSO-d₆)
 9.31 (br, 2H), 9.08 (br, 2H), 8.57 (t, 1H), 7.75 (d, 2H), 7.71 (d, 1H), 7.47 (d, 2H), 7.29 (m, 5H), 4.52-4.21
 (m, 3H), 3.54 (m, 2H), 3.28 (m, 2H), 3.04 (m, 1H), 2.90 (m, 2H), 2.71 (s, 3H), 2.50 (s, 3H), 1.88 (m, 2H)

20 IR: 3375, 1663, 1630, 1454, 1327, 1225, 1154, 1046

Example 5

4-Amidino-[(S)-N-[(R)-N'-methylsulfonylmethionyl] prolyl] aminomethylbenzene (compound No. 110 of Table 1) hydrochloride

NMR (DMSO-d₆)
 9.45 (br, 2H), 9.26 (br, 2H), 8.68 (t, 1H), 7.80 (d, 2H), 7.55 (d, 2H), 7.48 (d, 2H), 4.44-4.17 (m, 4H), 3.70
 (m, 1H), 3.59 (m, 1H), 2.87 (s, 3H), 2.56 (m, 3H), 2.13 (m, 1H), 2.08 (s, 3H), 1.97 - 1.63 (m, 4H)

30 IR: 3368, 1638, 1543, 1489, 1426, 1314, 1150

Example 6

4-Amidino-[(S)-N-((R)-N'-formylphenylalanyl) prolyl] aminomethylbenzene (compound No. 94 of Table 1) hydrochloride

NMR (DMSO-d₆)
 9.56 (br, 2H), 9.36 (br, 2H), 8.97 (t, 1H), 8.70 - 8.60 (m, 1H), 7.86 (d, 1H), 7.83 (d, 2H), 7.46 (d, 2H),
 7.37-7.17 (m, 5H), 4.36-4.16 (m, 4H), 3.60 - 2.70 (m, 4H), 2.40-1.20 (m, 4H)

40 IR: 3370, 1647, 1541, 1489, 1454, 1404, 704

Example 7

4-Amidino-[(S)-N-((R)-2-methylsulfonylamino-hexanoyl) prolyl] aminomethylbenzene (compound No. 109 of Table 1) methanesulfonate

NMR (DMSO-d₆)
 9.32 (br, 2H), 9.11 (br, 2H), 8.58 (t, 1H), 7.76 (d, 2H), 7.48 (d, 2H), 7.42 (d, 1H), 4.47-4.23 (m, 2H), 4.20-
 3.90 (m, 3H), 3.54-3.45 (m, 1H), 3.80-3.66 (m, 1H), 2.74 (s, 3H), 2.43 (s, 3H), 2.20-0.79 (m, 13H)

50 IR: 3272, 1638, 1543, 1424, 1316, 1206, 1155, 1047

Example 8

4-Amidino-[(S)-N-((R)-2-methylsulfonylamino-4-(4'-methoxy-carbonylphenyl) butanoyl) prolyl]-aminomethylbenzene (compound No. 127 of Table 1) hydrochloride

NMR (DMSO-d₆)
 9.35-9.23 (m, 4H), 8.59 (t, 1H), 7.90 (d, 2H), 7.77 (d, 2H), 7.61 (d, 1H), 7.47 (d, 2H), 7.40 (d, 2H), 4.44-

4.21 (m, 3H), 4.07 (m, 1H), 3.84 (s, 3H), 3.48 (m, 2H), 2.92-2.63 (m, 3H), 2.77 (s, 3H), 2.12 (m, 1H), 1.84 (m, 4H)
 IR: 3370, 1638, 1541, 1489, 1437, 1287, 1150

5 Example 9

4-Amidino-[(S)-N-[(R)-2-methylsulfonylamino-3-(3'-carboxyphenoxy) propanoyl] prolyl]aminomethylbenzene (compound No. 130 of Table 1) hydrochloride

10 NMR (DMSO-d⁶)

9.35 (br, 4H), 8.64 (t, 1H), 7.78 (d, 2H), 7.71 (d, 1H), 7.58-7.40 (m, 5H), 7.20 (m, 1H), 4.62 (m, 1H), 4.36 (m, 3H), 4.22 (m, 2H), 3.72 (m, 2H), 2.89 (s, 3H), 2.12 (m, 1H), 1.94 (m, 3H)
 IR: 3856, 1644, 1543, 1489, 1449, 1316, 1256, 1154

15 Example 10

4-Amidino-[(S)-N-[(R)-2-ethyisulfonylamino-3-(2'-benzyloxycarbonylphenoxy) propanoyl] prolyl]aminomethylbenzene (compound No. 123 of Table 1) hydrochloride

20 NMR (DMSO-d⁶)

9.24 (br, 4H), 8.60 (t, 1H), 7.77 (d, 2H), 7.71 (m, 1H), 7.57 (m, 1H), 7.49-7.35 (m, 8H), 7.16 (d, 1H), 7.07 (t, 1H), 5.29 (s, 2H), 4.62 (t, 1H), 4.37 (m, 3H), 4.28 (m, 1H), 4.17 (t, 1H), 3.67 (m, 2H), 2.91 (s, 3H), 2.15 (m, 1H), 1.88 (m, 3H)
 IR: 3366, 1642, 1491, 1451, 1314, 1248, 1082

25

Example 11

4-Amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-3-methyl-3-methylthiobutanoyl] prolyl]aminomethylbenzene (compound No. 98 of Table 1) hydrochloride

30

NMR (DMSO-d⁶)

8.89 (br, 2H), 8.66 (br, 2H), 7.77 (d, 2H), 7.33 (d, 2H), 6.27 (d, 1H), 4.65 (m, 1H), 4.46 (d, 1H), 4.37 (m, 2H), 3.97-3.72 (m, 4H), 2.62 (m, 1H), 2.15 (br, 3H), 2.04 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.05 (t, 3H)
 IR: 3323, 2926, 1635, 1535, 1439, 1242, 1055

35

Example 12

4-Amidino-[(S)-N-[(R)-2-carboxymethylsulfonylaminoheptanoyl] prolyl]aminomethylbenzene (compound No. 152 of Table 1) hydrochloride

40

NMR (DMSO-d⁶)

9.80 (br, 2H), 9.23 (br, 2H), 8.80 (t, 1H), 7.69 (d, 2H), 7.42 (d, 2H), 7.23 (d, 1H), 4.51-4.17 (m, 5H), 3.70 (m, H), 2.11 (m, 1H), 1.92 (m, 3H), 1.57-1.28 (m, 8H), 0.87 (m, 3H)
 IR: 3366, 2957, 1636, 1543, 1489, 1416, 1318, 1136

45

Example 13

4-Amidino-[(S)-N-(4-phenylbutanoyl)prolyl]aminomethylbenzene (compound No. 3 of Table 1) hydrochloride

50 NMR (DMSO-d⁶)

9.39 (br, 2H), 9.22 (br, 2H), 8.55 (t, 1H), 7.80 (d, 2H), 7.48 (d, 2H), 7.31-7.13 (m, 5H), 4.37-4.30 (m, 3H), 3.60-3.30 (m, 2H), 2.60 (t, 2H), 2.34-1.75 (m, 8H)
 IR: 3264, 1618, 1541, 1491, 1451, 702

Example 14

4-Amidino-[(S)-N-(2-benzyloxyacetyl)prolyl] aminomethylbenzene (compound No. 55 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

9.41 (br, 2H), 9.23 (br, 2H), 8.66 (t, 1H), 7.80 (d, 2H), 7.49 (d, 2H), 7.42-7.27 (m, 5H), 4.61-4.08 (m, 7H),
3.56-3.40 (m, 2H), 2.20-1.78 (m, 4H)

IR: 3262, 1645, 1539, 1489, 1454, 740

10 Example 15

Trans-4-amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl]prolyl] aminomethylcyclohexane (compound No. 263 of Table 1) hydrochloride

15 (a) Trans-4-N-benzyloxycarbonylaminomethyl-cyclohexyl nitrile

To a solution of trans-4-aminomethylcyclohexanecarboxylic acid (25 g, 159 mmol) and sodium carbonate (20 g, 191 mmol) in water (300 ml), benzyloxycarbonyl chloride (27 ml, 190 mmol) is added at 0 °C.

20 After stirring for 6 hours, 1N-hydrochloric acid is added until the pH of the reaction mixture indicates 2, and the precipitated white solid is collected, washed with water and dried. The resulting white solid is dissolved in THF (300 ml) and CDI (21 g, 130 mmol) is added at 0 °C. After stirring for 3 hours, the reaction mixture is added dropwise to a mixed solution of 33% ammonia in water (50 ml) and THF (150 ml) at 0 °C. After stirring for 5 hours, the solvent is evaporated and water (500 ml) is added, and the precipitated white solid is collected, washed with water and dried.

25 To a solution of the resulting compound in 1,2-dichloroethane (500 ml), thionyl chloride (19 ml, 260 mmol) is added and heated to an inner temperature of 70 °C. After stirring for 5 hours, the reaction mixture is poured into ice water and neutralized with an aqueous 1N-sodium hydroxide solution. After extracting with chloroform, the organic layer is washed twice with water and once with saturated brine, successively, and 30 then dried over sodium sulfate. The solvent is evaporated and the resulting crude product is recrystallized (hexane-ethyl acetate) to give 22.8 g of the titled compound (53%). mp: 90-92 °C

(b) Trans-4-(S)-prolylaminomethyl-cyclohexyl nitrile

35 The compound obtained in the item (a) is dissolved in ethanol (250 ml) and the catalytic hydrogenation is conducted at room temperature and atmospheric pressure in the presence of palladium black (1 g). After the completion of the reaction, the catalyst is filtered off and the solvent is evaporated.

To a solution of (S)-N-benzyloxycarbonylproline (20.7 g, 83 mmol) in THF (150 ml), CDI (13.5 g, 83 mmol) is added at 0 °C. After stirring for 3 hours, a solution of the compound obtained in the above reaction 40 in THF (200 ml) is added at 0 °C. After stirring for 12 hours, the solvent is evaporated, and chloroform (400 ml) is added to the resulting residue. The organic layer is washed three times with water and once with saturated brine, successively, and then dried over sodium sulfate. The solvent is evaporated and the resulting residue is purified with silica gel chromatography (chloroform-methanol).

The resulting compound is dissolved in ethanol (250 ml) and the catalytic hydrogenation is conducted 45 at room temperature and atmospheric pressure in the presence of palladium black (1 g). After the completion of the reaction, the catalyst is filtered off and the solvent is evaporated to give 18.8 g of the titled compound (95%).

NMR (DMSO-d₆)

0.88-1.06 (m, 2H), 1.38-1.52 (m, 3H), 1.68-2.03 (m, 7H), 2.20-2.40 (m, 1H), 2.52-2.67 (m, 1H), 2.80-3.20 50 (m, 4H), 4.03-4.10 (m, 1H), 7.53 (br, 1H), 8.65-8.70 (m, 1H)

(c) Trans-4-amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]-aminomethylcyclohexane hydrochloride

55 According to the same manner as that described in the items (c) to (e) of Example 1, the titled compound can be synthesized from the compound obtained in the item (b) and (R)-2-t-butylcarbonylamino-4,4-dimethylpentanoic acid.

NMR (DMSO-d₆)

8.95 (br, 2H), 8.69 (br, 2H), 7.60 (br, 1H), 6.32 (br, 1H), 4.56 (m, 1H), 4.39 (m, 1H), 4.18 (q, 2H), 4.10 (m, 1H), 3.52 (m, 1H), 3.19 (m, 1H), 2.89 (m, 1H), 2.69 (m, 1H), 2.14-1.59 (m, 12H), 1.26 (t, 3H), 0.98 (s, 9H), 0.98-0.89 (m, 2H)

IR: 3314, 2954, 1686, 1639, 1543, 1449, 1250, 1059

5 According to the same procedures, the compounds shown in the following Examples were synthesized.

Example 16

Trans-4-amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-3-cyclohexylpropanoyl] prolyl]aminoethylcyclohexane
10 (compound No. 227 of Table 1) hydrochloride

NMR (DMSO-d⁶)

8.93 (br, 2H), 8.81 (br, 2H), 7.53 (br, 1H), 7.38 (t, 1H), 4.50-4.15 (m, 1H), 4.10-3.90 (m, 2H), 3.73-3.17 (m, 2H), 3.05-2.80 (m, 3H), 2.39 (br, 1H), 2.00-0.68 (m, 29H)

15 IR: 3297, 2926, 2853, 1684, 1543, 1449, 1262, 1053

Example 17

Trans-4-amidino-[(S)-N-[(R)-2-isopropoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]-
20 aminomethylcyclohexane (compound No. 265 of Table 1) hydrochloride

NMR (DMSO-d⁶)

8.91 (br, 2H), 8.78 (br, 2H), 7.55 (br, 1H), 7.28 (t, 1H), 4.78-4.70 (m, 1H), 4.30-3.92 (m, 1H), 3.80-3.20 (m, 3H), 3.0-2.75 (m, 2H), 2.50-1.37 (m, 14H), 1.18-1.00 (m, 6H), 1.0-0.81 (m, 1H)

25 IR: 3285, 2953, 2870, 1684, 1541, 1449, 1250, 1111

Example 18

Trans-4-amidino-[(S)-N-((R)-N'-methylsulfonylphenylalanyl) prolyl] aminomethylcyclohexane (compound No.
30 250 of Table 1) hydrochloride

NMR (DMSO-d⁶)

8.88 (br, 2H), 8.75 (br, 2H), 7.85 (t, 1H), 7.65 (d, 1H), 4.27 (m, 1H), 4.16 (m, 1H), 3.51-3.41 (m, 4H), 2.99-2.70 (m, 4H), 2.78 (s, 3H), 2.38 (t, 1H), 1.90-1.40 (m, 9H), 1.08-0.87 (m, 2H)

35 IR: 3375, 2930, 1637, 1452, 1309, 1149, 1097, 983

Example 19

Trans-4-amidino-[(S)-N-((R)-N'-methylsulfonylleucyl) prolyl] aminomethylcyclohexane (compound No. 269 of
40 Table 1) hydrochloride

NMR (DMSO-d⁶)

8.89 (br, 2H), 8.85 (br, 2H), 6.56 (d, 1H), 4.53 (m, 1H), 4.17 (m, 1H), 3.86 (m, 1H), 3.47 (m, 1H), 3.07 (m, 2H), 2.97 (s, 3H), 2.13-1.80 (m, 10H), 1.63-1.54 (m, 4H), 1.33 (m, 1H), 0.98-0.87 (m, 2H), 0.97 (d, 6H)

45 IR: 3261, 2932, 1639, 1450, 1313, 1143, 1087, 985

Example 20

Trans-4-amidino-[(S)-N-((R)-2-methylsulfonylamino-3-cyclohexylpropanoyl) prolyl]aminomethylcyclohexane
50 (compound No. 230 of Table 1) hydrochloride

NMR (DMSO-d⁶)

8.95 (br, 2H), 8.53 (br, 2H), 7.27 (m, 1H), 6.51 (d, 1H), 4.51 (m, 1H), 4.19 (m, 1H), 3.83 (m, 1H), 3.66 (m, 1H), 3.41 (m, 2H), 3.04 (m, 2H), 3.04 (m, 2H), 2.95 (s, 3H), 2.46 (t, 1H), 2.12-0.92 (m, 24H)

55 IR: 3265, 2926, 1639, 1545, 1448, 1315, 1143, 985

Example 21

Trans-4-amidino-[(S)-N-((R)-2-isopropoxycarbonylamino-2-cyclohexylacetyl) prolyl]aminomethylcyclohexane (compound No. 228 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

8.91 (br, 2H), 8.69 (br, 2H), 7.36 (br, 1H), 5.99 (d, 1H), 4.84-4.79 (m, 1H), 4.58 (br, 2H), 4.53-4.50 (m, 2H), 4.10-3.90 (m, 2H), 3.60-3.40 (m, 1H), 2.50-0.97 (m, 30H)

IR: 3297, 2980, 2930, 2855, 1684, 1539, 1451, 1258

10 Example 22

Trans-4-amidino-[(S)-N-((R)-2-ethoxycarbonylamino-4-ethyl-hexanoyl) prolyl]aminomethylcyclohexane (compound No. 264 of Table 1) hydrochloride

15 NMR (DMSO-d₆)

8.91 (br, 2H), 8.70 (br, 2H), 7.54 (m, 1H), 6.34 (m, 1H), 4.56 (m, 1H), 4.38 (m, 1H), 4.11 (m, 3H), 3.48 (m, 1H), 3.21 (m, 1H), 2.88 (m, 1H), 2.68 (m, 1H), 2.30-1.19 (m, 18H), 1.26 (t, 3H), 0.96 (m, 2H), 0.86 (t, 6H)

IR: 3279, 2962, 1685, 1639, 1541, 1448, 1257, 1059, 752

20 Example 23

Trans-4-amidino-[(S)-N-[(R)-2-t-butoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]aminomethylcyclohexane (compound No. 266 of Table 1) glycolate

25 NMR (DMSO-d₆)

9.54 (br, 2H), 8.72 (br, 2H), 7.54 (br, 1H), 7.01 (t, 1H), 4.60-4.00 (m, 4H), 3.40 (m, 2H), 3.10-2.75 (m, 3H), 2.35 (br, 1H), 2.00-1.20 (m, 24H), 0.91 (s, 9H)

IR: 3316, 2953, 1686, 1543, 1449, 1368, 1167

30 Example 24

4-[(S)-N-[(R)-2-t-butyloxycarbonylamino-cyclohexylacetyl] prolyl] aminomethyl-benzamidoxime (compound No. 396 of Table 1)

35 To a solution of the compound (0.94 g, 2 mmol) obtained in the item (c) of Example 1 in ethanol (15 ml), a solution of sodium carbonate (0.17 g, 1.6 mmol) in water (3 ml) and hydroxyamine hydrochloride (0.22 g, 3.2 mmol) are added. After the reaction mixture is heated at reflux for 8 hours, the solvent is evaporated and the resulting residue is purified with silica gel column chromatography (chloroform-methanol) to give 0.84 g of the titled compound (84%).

40 NMR (CDCl₃)

1.0-1.49 (m, 14H), 1.5-2.4 (m, 10H), 3.56 (br, 1H), 3.97 (br, 1H), 4.09 (t, 1H), 4.41 (dq, 2H), 4.67 (d, 1H), 4.94 (br, 2H), 5.41 (d, 1H), 7.20 (d, 2H), 7.23-7.27 (m, 1H), 7.50 (d, 2H), 7.75 (br, 1H)

IR: 3345, 2978, 2930, 2855, 1640, 1528, 1449, 1167

45 According to the same procedures, the compounds shown in the following Examples were synthesized.

Example 25

4-[(S)-N-phenylacetylprolyl] aminomethyl-benzamidoxime (compound No. 374 of Table 1)

50 NMR (CDCl₃)

8.11 (t, 1H), 7.37 (d, 2H), 7.28-7.23 (m, 5H), 7.08 (d, 2H), 4.88 (s, 2H), 4.68 (d, 1H), 4.51 (m, 1H), 4.21 (m, 1H), 3.71 (s, 2H), 3.63-3.51 (m, 2H), 2.40-2.01 (m, 4H)

IR: 3315, 2968, 1637, 1543, 1244, 1155, 927, 709

Example 26

4-[(S)-N-[(R)-N'-ethoxycarbonylphenyl]alanyl] prolyl]aminomethylbenzamidoxime (compound No. 387 of Table 1)

5 NMR (CDCl₃)

7.54 (d, 2H), 7.27-7.19 (m, 7H), 6.31 (d, 1H), 5.05 (br, 2H), 4.65-4.42 (m, 3H), 4.24-4.10 (m, 1H), 3.80-3.40 (m, 3H), 3.10-2.95 (m, 2H), 2.60-2.50 (m, 1H), 2.14 (br, 1H), 1.95-1.50 (m, 3H), 0.99 (t, 3H)

IR: 3339, 1641, 1539, 1451, 1260, 752, 702

10 Example 27

4-[(S)-N-[(R)-2-t-butyloxycarbonylamino-3-cyclohexylpropanoyl] prolyl]aminomethylbenzamidoxime (compound No. 397 of Table 1)

15 NMR (CDCl₃)

7.75 (br, 1H), 7.50 (d, 2H), 7.21 (d, 2H), 5.40 (d, 1H), 4.94 (br, 2H), 4.64 (br, 1H), 4.40-4.25 (m, 3H), 3.95 (br, 1H), 3.50-3.40 (m, 1H), 2.0-0.80 (m, 26H)

IR: 3337, 2978, 2924, 2851, 1642, 1536, 1449, 1167

20 Example 28

4-[(S)-N-[(R)-2-ethoxycarbonylamino-3-methyl-3-methylthiobutanoyl] prolyl]aminomethylbenzamidoxime (compound No. 419 of Table 1)

25 NMR (CDCl₃)

7.66 (t, 1H), 7.53 (d, 2H), 7.23 (d, 2H), 5.64 (d, 1H), 4.91 (s, 2H), 4.68 (d, 1H), 4.58-4.30 (m, 3H), 3.90 (m, 1H), 3.87-3.76 (m, 2H), 3.62 (m, 1H), 2.37 (m, 1H), 2.09-2.00 (m, 3H), 2.06 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.09 (t, 3H)

30 IR: 3339, 2978, 1641, 1535, 1439, 1249, 1057, 929, 754

Example 29

4-[(S)-N-[(R)-phenylalanyl] prolyl]aminomethylbenzamidoxime (compound No. 390 of Table 1) dihydrochloride

NMR (DMSO-d₆)

11.24 (br, 1H), 9.02 (br, 2H), 8.91 (t, 1H), 8.80 (br, 3H), 7.66 (d, 2H), 7.44 (d, 2H), 7.35-7.22 (m, 5H), 4.30-4.16 (m, 4H), 3.57-2.95 (m, 3H), 2.45-2.30 (m, 1H), 1.90-1.20 (m, 4H)

40 IR: 3059, 1649, 1539, 1491, 1454

Example 30

Trans-4-[(S)-N-[(R)-2-isopropoxycarbonylamino-2-cyclohexylacetyl] prolyl]aminomethylcyclohexanecarboxamidoxime (compound No. 430 of Table 1)

NMR (CDCl₃)

7.14 (br, 1H), 5.70 (d, 1H), 4.85-4.80 (m, 1H), 4.70-4.50 (m, 3H), 4.17-4.08 (m, 2H), 3.96 (br, 1H), 3.54 (q, 1H), 3.05 (t, 2H), 2.40-2.20 (m, 1H), 2.09-0.88 (m, 30H)

50 IR: 3342, 2978, 2928, 2855, 1653, 1449, 1256, 1111

Example 31

Trans-4-[(S)-N-[(R)-2-t-butoxycarbonylamino-3-cyclohexylpropanoyl] prolyl]aminomethylcyclohexanecarboxamidoxime (compound No. 435 of Table 1)

NMR (CDCl₃)

7.14 (br, 1H), 5.40 (d, 1H), 4.60-4.33 (m, 5H), 3.88 (br, 1H), 3.43 (q, 1H), 3.20-3.11 (m, 1H), 3.0-2.96 (m,

1H), 2.40-2.30 (m, 1H), 2.0-0.84 (m, 35H)
 IR: 3356, 2926, 2853, 1649, 1537, 1448, 1167

Example 32

5 Trans-4-[(S)-N-[(R)-2-t-butoxycarbonylamino-2-cyclohexylacetyl]-
 aminomethylcyclohexanecarboxamidoxime (compound No. 433 of Table 1) prolyl]-

10 NMR (CDCl₃)
 7.15 (br, 1H), 5.28 (d, 1H), 4.58 (br, 4H), 4.09 (t, 1H), 3.92 (br, 1H), 3.53 (q, 1H), 3.20-2.90 (m, 2H), 2.40
 (br, 1H), 2.10-0.91 (m, 33H)
 IR: 3347, 2930, 2855, 1649, 1541, 1451, 1169

Example 33

15 Trans-4-[(S)-N-[(R)-2-t-ethoxycarbonylamino-4,4-dimethylpentanoyl]-
 aminomethylcyclohexanecarboxamidoxime (compound No. 461 of Table 1) prolyl]-

NMR (CDCl₃)
 20 7.06 (t, 1H), 5.56 (d, 1H), 4.57-4.39 (m, 4H), 4.11 (q, 2H), 3.98 (m, 1H), 3.47 (m, 1H), 3.05 (m, 2H), 2.39
 (m, 1H), 2.04-1.78 (m, 10H), 1.57 (d, 2H), 1.56-1.12 (m, 2H), 1.24 (t, 3H), 0.99 (s, 9H), 0.99-0.89 (m, 2H)
 IR: 3356, 2934, 1649, 1541, 1446, 1249, 1059, 927

Example 34

25 Trans-4-[(S)-N-[(R)-2-methoxycarbonylamino-4,4-dimethylpentanoyl]-
 aminomethylcyclohexanecarboxamidoxime (compound No. 458 of Table 1) prolyl]-

NMR (CDCl₃)
 30 7.04 (t, 1H), 5.53 (d, 1H), 4.68 (s, 2H), 4.56 (d, 1H), 4.43 (m, 1H), 3.98 (m, 1H), 3.66 (s, 3H), 3.47 (m,
 1H), 3.07 (m, 2H), 2.39 (m, 1H), 2.19-1.77 (m, 8H), 1.57 (d, 2H), 1.55-1.25 (m, 4H), 0.99 (s, 9H), 0.93 (m,
 2H)
 IR: 3344, 2949, 1712, 1649, 1548, 1448, 1249, 1059

Example 35

Trans-4-[(S)-N-[(R)-2-t-butoxycarbonylamino-4,4-dimethylpentanoyl]-
 aminomethylcyclohexanecarboxamidoxime (compound No. 467 of Table 1) prolyl]-

40 NMR (CDCl₃)
 7.12 (t, 1H), 5.14 (d, 1H), 4.58 (d, 1H), 4.53 (s, 2H), 4.37 (m, 1H), 3.92 (m, 1H), 3.45 (m, 1H), 3.19 (m,
 1H), 2.95 (m, 1H), 2.42 (m, 1H), 2.06-1.79 (m, 8H), 1.53 (d, 2H), 1.52-1.34 (m, 4H), 1.43 (s, 9H), 0.99 (s, 9H),
 1.00-0.89 (m, 2H)
 IR: 3358, 2930, 1649, 1535, 1448, 1367, 1249, 1168

Example 36

Trans-4-[(S)-N-[(R)-2-benzyloxycarbonylamino-4,4-dimethylpentanoyl]-
 aminomethylcyclohexanecarboxamidoxime (compound No. 469 of Table 1) prolyl]-

50 NMR (CDCl₃)
 7.36-7.27 (m, 5H), 7.04 (t, 1H), 5.63 (d, 1H), 5.16-5.00 (m, 2H), 4.58-4.46 (m, 4H), 3.97 (m, 1H), 3.47 (m,
 1H), 3.06-2.92 (m, 2H), 2.43-2.38 (m, 1H), 2.01-1.72 (m, 8H), 1.58 (d, 2H), 1.50-1.23 (m, 4H), 0.98 (s, 9H),
 0.98-0.88 (m, 2H)
 55 IR: 3356, 2928, 1649, 1541, 1448, 1249, 1053 929

Example 37

Trans-4-[(S)-N-[(R)-2-isopropoxycarbonylamino-4,4-dimethylpentanoyl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 464 of Table 1)

5 NMR (CDCl₃)
7.11 (t, 1H), 5.49 (d, 1H), 4.83 (m, 1H), 4.56 (m, 3H), 4.42 (dd, 1H), 3.98 (m, 1H), 3.47 (dd, 1H), 3.04 (m, 2H), 2.40 (m, 1H), 2.01 (m, 2H), 1.92 (m, 3H), 1.80 (m, 3H), 1.57 (d, 2H), 1.39 (m, 4H), 1.21 (m, 6H), 0.99 (s, 9H), 0.94 (m, 2H)

10 IR: 3343, 1649, 1541, 1449, 1275

Example 38

Trans-4-[(S)-N-[(R)-2-isopropoxycarbonylamino-2-cyclopentylacetyl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 464 of Table 1)

NMR (CDCl₃)
7.14 (t, 1H), 5.42 (d, 1H), 4.83 (m, 1H), 4.60 (d, 1H), 4.52 (s, 2H), 4.13 (m, 1H), 3.98 (m, 1H), 3.56 (m, 1H), 3.04 (m, 2H), 2.35 (m, 1H), 2.24 (m, 1H), 2.10-1.30 (m, 20H), 1.23 (dd, 6H), 1.01-0.93 (m, 2H)

20 IR: 3344, 2934, 1649, 1541, 1448, 1275, 1111, 754

Example 39

Trans-4-[(S)-N-[(R)-2-t-butoxycarbonylamino-2-cyclopentylacetyl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 432 of Table 1)

NMR (CDCl₃)
7.16 (t, 1H), 5.16 (d, 1H), 4.60 (d, 1H), 4.51 (s, 2H), 4.14 (t, 1H), 3.94 (m, 1H), 3.52 (m, 1H), 3.01 (m, 2H), 2.38 (m, 1H), 2.23-1.39 (m, 21H), 1.43 (s, 9H), 1.17-0.90 (m, 2H)

30 IR: 3350, 2932, 1649, 1541, 1448, 1367, 1251, 1167, 929

Example 40

Trans-4-[(S)-N-[(R)-2-ethoxycarbonylamino-3-cyclohexylpropanoyl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 428 of Table 1)

NMR (CDCl₃)
7.08 (br, 1H), 5.53 (d, 1H), 4.80-4.40 (m, 4H), 4.10-3.85 (m, 4H), 3.44 (q, 1H), 3.06 (t, 3H), 2.15-0.90 (m, 29H)

40 IR: 3343, 2926, 2853, 1649, 1541, 1449, 1260, 1053

Example 41

Trans-4-[(S)-N-[(R)-2-isopropoxycarbonylamino-3-cyclohexylpropanoyl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 431 of Table 1)

NMR (CDCl₃)
7.12 (br, 1H), 5.51 (d, 1H), 4.85-4.70 (m, 1H), 4.60-4.30 (m, 4H), 4.0-3.85 (m, 1H), 3.44 (q, 1H), 3.10-2.95 (m, 3H), 2.45-2.35 (m, 1H), 2.05-0.80 (m, 32H)

50 IR: 3347, 2978, 2926, 2853, 1649, 1539, 1449, 1261, 1111

Example 42

Trans-4-[(S)-N-[(R)-2-isopropoxycarbonylamino-4-ethyl-hexanoyl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 463 of Table 1)

NMR (CDCl₃)
7.11 (t, 1H), 5.41 (d, 1H), 4.83 (m, 1H), 4.56 (m, 3H), 4.39 (m, 1H), 3.94 (m, 1H), 3.46 (m, 1H), 3.02 (m,

2H), 2.39 (m, 1H), 2.10-1.20 (m, 20H), 1.22 (dd, 6H), 1.02-0.84 (m, 2H), 0.86 (t, 6H)
 IR: 33346, 2962, 2930, 1653, 1541, 1448, 1271, 1113

Example 43

5 Trans-4-[(S)-N-((R)-2-t-butoxycarbonylamino-4-ethyl-hexanoyl) prolyl] aminomethylcyclohexanecarboxyamidoxime (compound No. 466 of Table 1)

NMR (CDCl₃)

10 7.19 (t, 1H), 5.14 (d, 1H), 4.60 (d, 1H), 4.50 (s, 2H), 4.33 (m, 1H), 3.89 (m, 1H), 3.43 (m, 1H), 3.15 (m, 1H), 2.95 (m, 1H), 2.40 (m, 1H), 2.10-1.19 (m, 20H), 1.43 (s, 9H), 1.04-0.89 (m, 2H), 0.86 (t, 6H)
 IR: 3346, 2964, 2930, 1649, 1541, 1448, 1367, 1280, 1251, 1168, 929

Example 44

15 Trans-4-[(S)-N-((R)-2-ethoxycarbonylamino-heptanoyl) prolyl] aminomethylcyclohexanecarboxyamidoxime (compound No. 459 of Table 1)

NMR (CDCl₃)

20 7.08 (t, 1H), 5.60 (d, 1H), 4.58 (m, 3H), 4.35 (m, 1H), 4.07 (m, 2H), 3.92 (m, 1H), 3.48 (m, 1H), 3.06 (m, 2H), 2.40 (m, 1H), 2.04-1.32 (m, 20H), 1.24 (t, 3H), 0.89 (t, 3H), 0.98 (m, 2H)
 IR: 3346, 2928, 1649, 1541, 1448, 1255, 1055, 927

Example 45

25 Trans-4-[(S)-N-((R)-N'-t-butoxycarbonylamino-methionyl) prolyl] aminomethylcyclohexanecarboxyamidoxime (compound No. 468 of Table 1)

NMR (CDCl₃)

30 7.07 (m, 1H), 5.31 (d, 1H), 4.55 (m, 4H), 3.56 (m, 1H), 3.10 (m, 2H), 2.57 (t, 2H), 2.37 (m, 1H), 2.11 (s, 3H), 2.06-1.29 (m, 14H), 1.43 (s, 9H), 1.00 (m, 2H)
 IR: 3354, 2928, 1647, 1541, 1448, 1367, 1251, 1167

Example 46

35 Trans-4-[(S)-N-((R)-2-hydroxy-4,4-dimethyl-pentanoyl) prolyl] aminomethylcyclohexanecarboxyamidoxime (compound No. 454 of Table 1)

NMR (CDCl₃)

40 7.19 (t, 1H), 4.68 (s, 2H), 4.50 (d, 1H), 4.36 (t, 1H), 3.64 (t, 1H), 3.39 (m, 1H), 3.06 (m, 2H), 2.35 (m, 2H), 2.16-1.79 (m, 9H), 1.44 (d, 2H), 1.43-1.25 (m, 3H), 1.00-0.95 (m, 2H), 1.02 (s, 9H)
 IR: 3337, 2944, 1653, 1620, 1566, 1448, 1386, 1248, 1087

Example 47

45 Trans-4-[(S)-N-((R)-2-ethoxycarbonylamino-4-ethyl-hexanoyl) prolyl] aminomethylcyclohexanecarboxyamidoxime (compound No. 460 of Table 1)

NMR (CDCl₃)

50 7.07 (t, 1H), 5.53 (d, 1H), 4.56 (m, 3H), 4.40 (m, 1H), 4.11 (q, 2H), 3.96 (m, 1H), 3.45 (m, 1H), 3.05 (m, 2H), 2.36 (m, 1H), 2.09-1.77 (m, 10H), 1.61-1.21 (m, 8H), 1.24 (t, 3H), 1.02-0.83 (m, 2H), 0.86 (t, 6H)
 IR: 3342, 2962, 2930, 1649, 1541, 1448, 1379, 1269, 1059, 929

Example 48

Trans-4-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl] aminomethylcyclohexanecarboxamide O-methoxycarbonyloxime (compound No. 531 of Table 1)

5

To a solution of the compound (4.2 g, 8.9 mmol) obtained in Example 33 and triethylamine (1.9 ml, 13.3 mmol) in dichloromethane (100 ml), a solution of methyl chloroformate (1.0 g, 10 mmol) in dichloromethane (10 ml) is added at 0°C. After stirring for 4 hours, the organic layer is washed once with an aqueous saturated sodium bicarbonate solution, water and saturated brine, successively. After drying over sodium sulfate, the solvent is evaporated and the residue is purified with silica gel column chromatography (ethyl acetate-methanol) to give 2.9 g of the titled compound (62%).

10 NMR (CDCl_3)

15 0.89-1.07 (m, 11H), 1.21-1.60 (m, 8H), 1.79-2.40 (m, 9H), 3.0-3.10 (m, 2H), 3.40-3.50 (m, 1H), 3.84 (s, 3H), 3.84-4.20 (m, 3H), 4.35-4.40 (m, 1H), 4.55 (d, 1H), 4.81 (br, 2H), 5.19 (d, 1H), 7.12 (t, 1H)

15 IR: 3345, 2953, 1763, 1699, 1645, 1541, 1443, 1256

According to the same procedures, the compounds shown in the following Examples were synthesized.

Example 49

20 4-[(S)-N-[(R)-2-hydroxy-2-cyclohexylacetyl] prolyl] aminomethylbenzamide O-ethoxycarbonyloxime (compound No. 543 of Table 1)

NMR (CDCl_3)

25 7.56 (d, 2H), 7.47 (t, 1H), 7.22 (d, 2H), 5.35 (s, 2H), 4.53 (m, 2H), 4.37 (d, 2H), 4.30 (q, 2H), 4.07 (m, 1H), 3.64 (m, 1H), 3.47 (m, 1H), 3.39 (m, 1H), 2.35-1.17 (m, 15H), 1.35 (t, 3H)

IR: 3368, 2928, 1772, 1628, 1554, 1452, 1404, 1228, 1087, 856

Example 50

30 Trans-4-[(S)-N-[(R)-2-hydroxy-4,4-dimethylpentanoyl] prolyl] aminomethylcyclohexanecarboxamide O-methoxycarbonyloxime (compound No. 534 of Table 1)

NMR (CDCl_3)

35 7.07 (t, 1H), 4.77 (s, 2H), 4.52 (d, 1H), 4.34 (m, 1H), 3.85 (s, 3H), 3.58 (t, 1H), 3.37 (m, 1H), 3.22 (d, 1H), 3.12-3.05 (m, 2H), 2.26-2.21 (m, 1H), 1.97-1.37 (m, 13H), 1.03 (s, 9H), 1.09-0.95 (m, 2H)

IR: 3346, 2953, 1763, 1643, 1442, 1257, 1089, 879

Example 51

40 Trans-4-[(S)-N-[(R)-2-hydroxy-4,4-dimethylpentanoyl] prolyl] aminomethylcyclohexanecarboxamide O-ethoxycarbonyloxime (compound No. 556 of Table 1)

NMR (CDCl_3)

45 7.05 (t, 1H), 4.73 (s, 2H), 4.52 (d, 1H), 4.34 (t, 1H), 4.27 (q, 2H), 3.58 (m, 1H), 3.45 (m, 1H), 3.08 (m, 2H), 2.44 (m, 1H), 2.30-1.30 (m, 13H), 1.32 (t, 3H), 1.03 (s, 9H), 1.07-0.92 (m, 2H)

IR: 3373, 2953, 1759, 1641, 1450, 1369, 1248, 1093

Example 52

50 Trans-4-amino-[(S)-N-[(R)-N'-methanesulfonylphenylanyl] prolyl] aminomethylcyclohexane (compound No. 776 of Table 1) L-tartrate.

(a) Trans-4-t-butyloxycarbonylamino-benzyloxycarbonylaminomethylcyclohexane

55 To a solution of trans-4-aminomethylcyclohexanecarboxylic acid (15.7 g, 100 mmol) and sodium hydroxide (4.0 g, 100 mmol) in water (30 ml), benzyloxycarbonyl chloride (15.6 ml, 110 mmol) and sodium hydroxide (4.4 g, 110 mmol) in water (30 ml) are added dropwise at 0°C, simultaneously. After stirring for 4 hours, the mixture is extracted once with ether and 1N-hydrochloric acid is added to the aqueous layer until

the pH of the mixture indicates 2. Then, the precipitated white solid is collected and dried.

To a solution of the resulting compound (12.8 g, 50 mmol) in t-butanol (150 ml), triethylamine (8.3 ml, 60 mmol) and OPPA (13.7 g, 50 mmol) are added and heated at reflux for 8 hours. After the solvent is evaporated, water is added to the residue and the mixture is extracted with chloroform. The organic layer is washed once with an aqueous sodium carbonate (5%), once with an aqueous potassium hydrogensulfate (5%), twice with water and once with saturated brine, successively, and then dried over sodium sulfate. The solvent is evaporated and the residue is purified with silica gel column chromatography (hexane-ethyl acetate) to give 8.6 g of the titled compound (47%).

NMR (CDCl₃)

0.85-1.37 (m, 14H), 1.60-1.85 (m, 4H), 2.84 (t, 1H), 3.12 (br, 1H), 5.00 (s, 2H), 6.62 (d, 1H), 7.23-7.39 (m, 6H)

(b) Trans-4-t-butyloxycarbonylamino-[(S)-N-butyloxycarbonylprolyl] aminomethylcyclohexane

The compound (4.4 g, 12 mmol) obtained in the item (a) is dissolved in methanol (200 ml) and the catalytic hydrogenation is conducted at room temperature and under atmospheric pressure in the presence of palladium black (0.4 g). After the completion of the reaction, the catalyst is filtered off and the solvent is evaporated.

To a solution of (S)-Z-proline (3.0 g, 12 mmol) in THF (30 ml), CDI (2.0 g, 12 mmol) is added at 0 °C. After stirring for 3 hours, a solution of the compound obtained in the above reaction in THF (150 ml) is added at 0 °C. After stirring for 6 hours, the solvent is evaporated and water (50 ml) is added to the residue. The mixture is extracted with chloroform and the organic layer is washed three times with water and once with saturated brine, successively. After drying over sodium sulfate, the solvent is evaporated and the residue is purified with silica gel chromatography (chloroform-methanol) to give 4.2 g of the titled compound (77%).

NMR (CDCl₃)

0.85-1.06 (m, 4H), 1.44 (s, 9H), 1.60-2.35 (m, 9H), 2.94-3.20 (m, 2H), 3.20-3.55 (m, 3H), 4.31 (br, 1H), 4.47 (br, 1H), 5.14 (s, 2H), 6.90 (br, 1H), 7.15-7.40 (m, 5H)

(c) Trans-4-t-butyloxycarbonylamino-[(S)-N-[(R)-N'-benzyloxycarbonylphenylalanyl] prolyl] aminomethylcyclohexane

The compound (3.6 g, 7.9 mmol) obtained in the item (b) is dissolved in methanol (50 ml) and the catalytic hydrogenation is conducted at room temperature and under atmospheric pressure in the presence of palladium black (0.3 g). After the completion of the reaction, the catalyst is filtered off and the solvent is evaporated.

To a solution of (R)-Z-phenylalanine (2.4 g, 7.9 mmol) in THF (30 ml), CDI (1.3 g, 7.9 mmol) is added at 0 °C. After stirring for 4 hours, a solution of the compound obtained in the above reaction in THF (60 ml) is added. After stirring for 8 hours, the solvent is evaporated and water is added to the reaction mixture. The mixture is extracted with chloroform and the organic layer is washed three times with water and once with saturated brine, successively, and then dried over sodium sulfate. The solvent is evaporated and the residue is purified with silica gel column chromatography (chloroform-methanol) to give 4.2 g of the titled compound (89%).

NMR (CDCl₃)

0.85-1.06 (m, 5H), 1.33-2.0 (m, 15H), 2.10-2.22 (m, 1H), 2.50-2.60 (m, 1H), 2.94-3.01 (m, 5H), 3.30 (br, 1H), 3.57 (t, 1H), 4.32-4.59 (m, 3H), 5.08 (d, 2H), 5.69 (d, 1H), 7.02 (br, 1H), 7.18-7.37 (m, 10H)

(d) Trans-4-amino-[(S)-N-[(R)-N'-methanesulfonylphenylalanyl]prolyl] aminomethylcyclohexane L-tartrate.

The compound (2.4 g, 3.9 mmol) obtained in the item (c) is dissolved in methanol (40 ml) and the catalytic hydrogenation is conducted at room temperature and under atmospheric pressure in the presence of palladium black (0.2 g). After the completion of the reaction, the catalyst is filtered off and the solvent is evaporated. To a solution of the resulting compound in dichloromethane (40 ml), triethylamine (0.65 ml, 4.7 mmol) is added and a solution of methanesulfonyl chloride (0.47 g, 4.1 mmol) in dichloromethane (100 ml) is further added at 0 °C. After stirring for 3 hours, an aqueous saturated sodium bicarbonate solution is added and the organic layer is washed once with water and saturated brine, successively. After drying over sodium sulfate, the solvent is evaporated and the residue is purified with silica gel chromatography (chloroform-methanol).

The resulting compound is dissolved in chloroform (10 ml) and a 4N-dioxane hydrochloride in dioxane (10 ml) is added at 0°C. After stirring for 2 hours, the solvent is evaporated and chloroform (10 ml) and a 1N-sodium hydroxide solution (10 ml) are added to the residue and, further, the mixture is stirred for 10 minutes. The organic layer is dried over sodium sulfate and a solution of L-tartaric acid (0.34 g, 2.26 nm) in 5 methanol (5 ml) is added.

The solvent is evaporated and ether (20 ml) is added, and then the precipitated white solid is collected and dried to give 1.36 g of the titled compound (58%).

NMR (DMSO-d₆)

7.77 (m, 4H), 7.28 (m, 5H), 4.28 (m, 1H), 4.16 (m, 1H), 3.57-3.45 (m, 8H), 2.73 (s, 3H), 1.91-1.75 (m, 10 9H), 1.54 (m, 1H), 1.25 (m, 4H), 0.93 (m, 2H)

IR: 3324, 2934, 1734, 1638, 1545, 1453, 1308, 1148

According to the same procedures, the compounds shown in the following Examples were synthesized.

Example 53

Trans-4-amino-[(S)-N-[(R)-2-methylsulfonylamino-2-cyclohexylacetyl] prolyl]aminomethylcyclohexane (compound No. 759 of Table 1) hydrochloride

NMR (DMSO-d₆)

20 8.09 (br, 3H), 7.80 (t, 1H), 7.39 (d, 1H), 4.30-4.26 (m, 1H), 3.87 (t, 1H), 3.80-3.45 (m, 2H), 3.0-2.80 (m, 3H), 2.85 (s, 3H), 2.10-0.80 (m, 24H)

IR: 3382, 2930, 2857, 1638, 1543, 1451, 1154

Example 54

25 Trans-4-amino-[(S)-N-[(S)-N'-benzenesulfonyl- α -glutamyl] prolyl] aminomethylcyclohexane (compound No. 792 of Table 1) hydrochloride

NMR (DMSO-d₆)

30 8.04 (br, 3H), 7.75-7.50 (m, 5H), 4.05 (q, 1H), 3.77-3.30 (m, 5H), 3.0-2.70 (m, 3H), 2.28 (t, 2H), 2.0-1.52 (m, 10H), 1.31-1.11 (m, 3H), 1.0-0.85 (m, 2H)

IR: 3400, 2937, 1637, 1449, 1161

Example 55

35 Trans-4-amino-[(S)-N-((RS)-3-methylsulfonylamino-3-phenylpropanoyl) prolyl]aminomethylcyclohexane (compound No. 777 of Table 1) hydrochloride

NMR (DMSO-d₆)

40 8.08 (m, 3H), 7.34 (m, 5H), 4.78 (m, 1H), 4.15 (m, 2H), 3.51 (m, 1H), 3.36 (m, 2H), 2.86 (m, 4H), 2.68 (s, 3H), 2.51 (m, 2H), 2.00-1.69 (m, 6H), 1.27 (m, 4H), 0.92 (m, 2H)

IR: 3409, 2936, 1638, 1453, 1314, 1148

Example 56

45 Trans-4-amino-[(S)-N-((R)-2-isopropoxycarbonylamino-4,4-dimethylpentanoyl) prolyl]-aminomethylcyclohexane (compound No. 797 of Table 1)

NMR (CDCl₃)

50 7.19 (m, 1H), 5.32 (d, 1H), 4.82 (m, 1H), 4.53 (m, 2H), 4.00 (m, 1H), 3.48 (m, 1H), 3.03-2.16 (m, 6H), 2.00-1.81 (m, 6H), 1.57 (d, 2H), 1.49 (m, 4H), 1.24 (m, 6H), 1.00 (s, 9H), 0.95 (m, 2H)

IR: 3326, 2949, 1640, 1541, 1449, 1248

Example 57

Trans-4-amino-[(S)-N-((R)-N'-ethoxycarbonyl-phenylalanyl) prolyl] aminomethylcyclohexane (compound No. 780 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

7.98 (m, 3H), 7.37 (t, 1H), 7.26 (m, 5H), 4.37 (dd, 1H), 4.16 (m, 1H), 4.02 (m, 2H), 3.88 (m, 1H), 3.59 (m, 1H), 3.43 (m, 1H), 2.86 (m, 5H), 1.93-1.75 (m, 7H), 1.28 (m, 4H), 1.15 (t, 3H), 0.92 (m, 2H)

IR: 3349, 2936, 1642, 1537, 1451, 1258

10 Example 58

Trans-4-amino-[(S)-((R)-phenylalanyl) prolyl]aminomethylcyclohexane (compound No. 779 of Table 1) hydrochloride

15 NMR (DMSO-d₆)

8.69 (br, 3H), 8.09 (br, 4H), 7.37-7.20 (m, 5H), 4.19 (br, 1H), 4.09-4.06 (m, 1H), 3.20-2.82 (m, 5H), 2.0-0.85 (m, 15H)

IR: 3426, 2936, 1649, 1539, 1497, 1454

20 Example 59

Trans-4-amino-[(S)-N-((R)-2-ethoxycarbonyloxy-3-phenylpropanoyl) prolyl]aminomethylcyclohexane (compound No. 785 of Table 1) hydrochloride

25 NMR (DMSO-d₆)

7.78 (m, 3H), 7.30 (m, 5H), 7.15 (d, 1H), 5.22 (t, 1H), 4.20 (m, 1H), 4.08 (m, 3H), 3.64 (m, 1H), 3.02-2.88 (m, 5H), 1.92-1.72 (m, 7H), 1.20-0.94 (m, 9H)

IR: 3397, 2938, 1740, 1655, 1453, 1269

30 Example 60

Trans-4-amino-[(S)-N-((R)-2-allylcaramoyloxy-3-phenylpropanoyl) prolyl]aminomethylcyclohexane (compound No. 787 of Table 1) hydrobromide

35 NMR (DMSO-d₆)

7.90 (m, 3H), 7.30 (m, 5H), 7.14 (m, 1H), 5.72 (m, 2H), 5.06 (m, 2H), 4.76 (m, 1H), 4.17 (m, 1H), 3.60 (m, 1H), 2.98-2.85 (m, 5H), 1.87-1.70 (m, 7H), 1.23 (m, 7H), 0.90 (m, 2H)

IR: 3364, 2936, 1707, 1645, 1543, 1454, 1256

40 Example 61

Trans-4-amino-[(S)-N-((R)-2-hydroxy-2-cyclohexylacetyl) prolyl] aminomethylcyclohexane (compound No. 768 of Table 1) hydrochloride

45 NMR (DMSO-d₆)

8.21 (br, 3H), 7.95 (m, 1H), 4.53 (m, 1H), 4.18 (d, 1H), 3.95 (m, 1H), 3.07 (m, 3H), 2.18-1.55 (m, 22H), 1.30-1.03 (m, 2H)

IR: 3422, 2928, 2854, 1637, 1450, 1388, 1240, 1114, 1045

50 Example 62

Trans-4-amino-[(S)-N-((R)-2-hydroxy-2-phenylacetyl) prolyl] aminomethylcyclohexane (compound No. 783 of Table 1) hydrochloride

55 NMR (DMSO-d₆)

7.98 (br, 3H), 7.37-7.28 (m, 5H), 5.48 (br, 1H), 5.23 (d, 1H), 4.23 (d, 1H), 3.70-3.35 (m, 2H), 3.0-2.80 (m, 4H), 2.0-1.60 (m, 8H), 1.40-0.90 (m, 5H)

IR: 3329, 2935, 1667, 1626, 1552, 1448

Example 63

5 Trans-4-amino-[(RS)-1-((R)-N'-methylsulfonyl-phenylalanyl)-2-piperidinocarboxyl]aminomethylcyclohexane (compound No. 834 of Table 1) hydrochloride

NMR (DMSO-d₆)

8.07 (m, 3H), 7.28 (m, 5H), 4.64 (m, 1H), 4.39 (m, 1H), 3.99 (m, 1H), 3.67 (m, 1H), 2.87 (m, 7H), 2.84 (s, 3H), 1.91-1.68 (m, 5H), 1.33-0.92 (m, 10H)
 10 IR: 3385, 2936, 1638, 1535, 1453, 1314, 1150

Example 64

15 Trans-4-amino-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]aminomethylcyclohexane (compound No. 794 of Table 1)

NMR (CDCl₃)

7.16 (m, 1H), 5.68 (d, 1H), 4.53 (d, 1H), 4.38 (m, 1H), 4.10 (q, 2H), 4.01 (m, 1H), 3.46-3.07 (m, 4H),
 20 2.30-1.81 (m, 8H), 1.58 (m, 5H), 1.26 (t, 3H), 1.00 (s, 9H), 0.95 (m, 2H)
 IR: 3329, 2949, 1642, 1541, 1447, 1248, 1059

Example 65

25 Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]aminomethylcyclohexane (compound No. 968 of Table 1)

To a solution of the compound (5.4 g, 11.7 mmol) obtained in Example 64 in DMF (40 ml), sodium carbonate (3.2 g, 23.4 mmol) is added, and a solution of 4-bromomethyl-5-methyl-1,3-dioxo-2-on (4.0 g, 30 17.6 mmol) in DMF (5 ml) is further added at 0 °C. After stirring for 48 hours, the solvent is evaporated and water is added to the residue, which is extracted with ethyl acetate. The organic layer is washed three times with water and once with saturated brine, successively, and then dried over sodium sulfate. The solvent is evaporated and the residue is purified with silica gel column chromatography (chloroform-methanol) to give 2.8 g of the titled compound (44%).

35 NMR (CDCl₃)

7.07 (m, 1H), 5.15 (d, 1H), 4.56 (d, 1H), 4.41 (m, 1H), 4.10 (q, 2H), 4.00 (m, 2H), 3.48 (s, 2H), 3.45 (m, 2H), 3.04 (t, 1H), 2.62 (m, 1H), 2.38 (m, 1H), 2.11 (s, 3H), 2.00 (m, 3H), 1.82 (m, 2H), 1.73-1.43 (m, 4H), 1.28 (t, 3H), 1.26 (m, 3H), 1.00 (s, 9H), 0.96 (m, 2H)
 IR: 3329, 2934, 2870, 1823, 1649, 1539, 1445, 1223

40 According to the same procedures, the compounds shown in the following Examples were synthesized.

Example 66

45 Trans-4-t-butoxycarbonylamino-[(S)-N-[(R)-N'-methanesulfonylphenylalanyl] prolyl]aminomethylcyclohexane (compound No. 955 of Table 1)

NMR (CDCl₃)

7.29 (m, 3H), 7.24 (m, 2H), 6.67 (t, 1H), 5.61 (d, 1H), 4.40 (m, 2H), 4.29 (dd, 1H), 3.58 (m, 1H), 3.34 (m, 1H), 2.99 (m, 4H), 2.82 (s, 3H), 2.69 (m, 1H), 2.18-1.74 (m, 9H), 1.43 (s, 9H), 1.02 (m, 4H)
 50 IR: 3376, 2932, 1655, 1526, 1453, 1322

Example 67

55 Trans-4-guanidino-[(S)-N-[(R)-N'-methanesulfonylphenylalanyl] prolyl]aminomethylcyclohexane (compound No. 646 of Table 1) sulfate

To a solution of the compound (0.45 g, 1 mmol) obtained in Example 52 in ethanol (15 ml), a solution of 2-methylisothiourea sulfate (0.14 g, 0.5 mmol) in water (5 ml) is added and heated at reflux for 6 hours. The

solvent is evaporated and ether (20 ml) is added. The precipitated white solid is collected and washed with ether, and then dried under reduced pressure to give 0.44 g of the titled compound (81%).

5 NMR (DMSO-d₆)
8.04-2.0 (m, 13H), 2.60-3.96 (m, 7H), 2.77 (s, 3H), 4.14-4.28 (m, 2H), 5.47 (br, 1H), 6.75 (br, 1H), 7.20-7.36 (m, 5H), 7.83 (br, 1H), 8.40 (br, 4H)

IR: 3322, 2932, 2193, 2153, 1644, 1545, 1451, 1319, 1150

According to the same procedure as that described in Example 1, the following compounds of Examples 68 to 78 were synthesized.

10 Example 68

4-Amidino-[(S)-N-[(R)-2-hydroxy-cyclohexylacetyl] prolyl] aminomethylbenzene (compound No. 82 of Table 1) hydrochloride

15 NMR (DMSO-d₆)
9.29 (br, 2H), 8.93 (br, 2H), 8.51 (t, 1H), 7.75 (d, 2H), 7.49 (d, 2H), 4.37 (m, 3H), 3.96 (d, 1H), 3.70 (m, 1H), 3.60-3.40 (m, 2H), 2.20-1.0 (m, 14H)
IR: 3227, 2922, 1657, 1607, 1539, 1485, 1458, 1323, 1246, 1032

20 Example 70

4-Amidino-[(S)-N-[(R)-2-methylsulfonylamino-3,3-dimethylbutanoyl] prolyl]aminomethylbenzene (compound No. 114 of Table 1) hydrochloride

25 NMR (DMSO-d₆)
9.24 (br, 2H), 8.63 (t, 1H), 7.81 (d, 2H), 7.47 (d, 2H), 7.20 (d, 1H), 4.42 (dd, 1H), 4.35 (t, 2H), 3.96 (d, 1H), 3.80-3.60 (m, 2H), 2.85 (s, 3H), 2.20-1.80 (m, 4H), 0.97 (s, 9H)
IR: 3273, 2970, 2365, 1630, 1541, 1483, 1412, 1304, 1153, 715

30 Example 70

4-Amidino-[(S)-N-[(R)-2-methylsulfonylamino-6-ethoxycarbonylhexanoyl] prolyl]aminomethylbenzene (compound No. 117 of Table 1) hydrochloride

35 NMR (DMSO-d₆)
9.35 (br, 4H), 8.66 (t, 1H), 7.79 (d, 1H), 7.48 (d, 2H), 4.35 (m, 3H), 4.65 (q, 2H), 3.69 (m, 1H), 3.55 (m, 1H), 2.75 (s, 3H), 2.29 (t, 2H), 2.13 (m, 2H), 1.94 (m, 2H), 1.85 (m, 2H), 1.52 (m, 7H), 1.18 (t, 3H)
IR: 3382, 1644, 1547, 1427, 1375, 1314, 1150, 1111

40 Example 71

4-Amidino-[(S)-N-[(R)-2-methylsulfonylamino-4-(3'-carboxy)-phenylbutanoyl] prolyl]aminomethylbenzene (compound No. 119 of Table 1) hydrochloride

45 NMR (DMSO-d₆)
9.45 (s, 2H), 9.38 (s, 2H), 8.62 (t, 1H), 7.84 (m, 2H), 7.79 (d, 2H), 7.64 (d, 1H), 7.47 (d, 2H), 7.42 (m, 2H), 4.33 (m, 3H), 4.10 (m, 1H), 3.57-3.37 (m, 2H), 2.85 (m, 1H), 2.78 (s, 3H), 2.73 (m, 1H), 2.12 (m, 1H), 1.95-1.81 (m, 6H)
IR: 3366, 1638, 1543, 1489, 1449, 1311, 1150, 754, 527

50 Example 72

4-Amidino-[(S)-N-[(R)-N'-methylsulfonyl-O-(4'-carboxyphenyl)-seryl] prolyl]aminomethylbenzene (compound No. 970 of Table 1) hydrochloride

55 NMR (DMSO-d₆)
9.31 (s, 2H), 9.00 (s, 2H), 8.59 (t, 1H), 7.90 (d, 2H), 7.83 (d, 1H), 7.75 (d, 2H), 7.48 (d, 2H), 7.03 (d, 2H), 4.35 (m, 4H), 4.22 (m, 2H), 4.12 (dd, 1H), 3.72 (m, 2H), 2.89 (s, 3H), 2.20-1.80 (m, 4H)

IR: 3376, 1647, 1607, 1424, 1318, 1252, 1154, 1119, 774, 633, 525

Example 73

5 4-Amidino-[(S)-N-[(R)-N'-methylsulfonyl-O-ethoxycarbonylmethyl-tyrosyl] prolyl]aminomethylbenzene (compound No. 971 of Table 1) hydrochloride

NMR (DMSO-d₆)

10 9.41 (br, 2H), 9.20 (br, 2H), 8.56 (t, 1H), 7.80 (d, 2H), 7.65 (d, 1H), 7.48 (d, 2H), 7.18 (dd, 2H), 6.84 (dd, 2H), 4.75 (q, 1H), 4.30 (dd, 1H), 4.30-4.25 (m, 2H), 3.70-3.42 (m, 3H), 3.47 (q, 2H), 3.18 (t, 1H), 2.83 (d, 2H), 2.72 (s, 3H), 1.89-1.60 (m, 4H), 1.14 (dt, 3H)

IR: 3370, 2365, 1742, 1636, 1541, 1512, 1445, 1308

Example 74

15 4-Amidino-[(S)-N-[(R)-N'-ethoxycarbonylphenylalanyl] prolyl] aminomethylbenzene (compound No. 972 of Table 1) hydrochloride

NMR (DMSO-d₆)

20 9.40 (br, 2H), 9.24 (br, 2H), 8.14 (t, 1H), 7.80 (d, 2H), 7.59 (t, 1H), 7.45 (d, 2H), 7.31-7.15 (m, 5H), 4.50-4.26 (m, 4H), 3.90-3.57 (m, 3H), 3.0-2.7 (m, 3H), 1.9-1.6 (m, 4H), 1.10-1.0 (m, 3H)

IR: 3279, 2364, 1637, 1539, 1491, 1450, 1255, 704

Example 75

25 4-Amidino-[(S)-N-[(R)-2-methylsulfonylaminohexanoyl] prolyl] aminomethylbenzene (compound No. 973 of Table 1) hydrochloride

NMR (DMSO-d₆)

30 9.37 (s, 2H), 9.16 (s, 2H), 8.60 (t, 1H), 7.76 (d, 2H), 7.48 (d, 2H), 7.40 (d, 1H), 4.50-4.23 (m, 3H), 4.08 (m, 1H), 3.69 (m, 1H), 3.36 (m, 1H), 2.74 (s, 3H), 2.15 (m, 1H), 2.09-1.84 (m, 3H), 1.61-1.22 (m, 8H), 0.87 (m, 3H)

IR: 3366, 2957, 1638, 1543, 1489, 1426, 1314, 1154, 718, 527

35 Example 76

4-Amidino-[(S)-N-[(R)-N'-methylsulfonyl-O-(3'-carboxymethyl-phenyl)-seryl] prolyl]aminomethylbenzene (compound No. 974 of Table 1) hydrochloride

40 NMR (DMSO-d₆)

9.46 (s, 2H), 9.31 (s, 2H), 8.70 (t, 1H), 7.83 (m, 3H), 7.48 (d, 2H), 7.19 (m, 2H), 6.89 (d, 2H), 4.58 (dd, 1H), 4.37 (m, 4H), 4.14 (d, 2H), 3.70 (m, 1H), 3.60 (m, 3H), 2.89 (s, 3H), 2.11 (m, 1H), 2.01-1.82 (m, 3H)

IR: 3382, 1724, 1640, 1543, 1489, 1447, 1316, 1262, 1154, 768, 527

45 Example 77

4-Amidino-[(S)-N-[(R)-N'-methylsulfonyl-O-(4'-carboxymethyl-phenyl)-seryl] prolyl]aminomethylbenzene (compound No. 975 of Table 1) hydrochloride

50 NMR (DMSO-d₆)

9.45 (s, 2H), 9.29 (s, 2H), 8.70 (t, 1H), 7.83 (d, 2H), 7.82 (d, 2H), 7.48 (d, 2H), 7.24 (d, 1H), 6.82 (d, 2H), 4.59 (dd, 1H), 4.37 (m, 4H), 4.14 (d, 2H), 3.70 (m, 1H), 3.61 (m, 3H), 2.89 (s, 3H), 2.11 (m, 1H), 2.01-1.82 (m, 3H)

IR: 3383, 1640, 1545, 1514, 1437, 1312, 1242, 1152, 824, 523

Example 78

4-Amidino-[(S)-N-[(R)-2-ethoxycarbonylmethylsulfonylamino-heptanoyl] prolyl]aminomethylbenzene (compound No. 976 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

9.36 (s, 2H), 9.15 (s, 2H), 8.49 (t, 1H), 7.81 (d, 1H), 7.77 (d, 2H), 7.47 (d, 2H), 4.35 (m, 3H), 4.21 (d, 1H), 4.15 (m, 1H), 4.06 (q, 2H), 3.93 (d, 1H), 3.73 (m, 1H), 3.53 (m, 1H), 2.14 (m, 1H), 1.94 (m, 3H), 1.67-1.18 (m, 8H), 1.14 (t, 3H), 0.89 (m, 3H)

10 IR: 3274, 2957, 2972, 1821, 1738, 1647, 1541, 1422, 1319, 1159, 1022, 723, 628, 527

According to the same procedures as that described in Example 15, the following compounds of Examples 79 to 86 were synthesized.

15 Example 79

Trans-4-amidino-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-butyloxy-seryl]prolyl] aminomethylcyclohexane (compound No. 240 of Table 1) hydrochloride

20 NMR (DMSO-d₆)

8.88 (br, 2H), 8.71 (br, 2H), 7.72 (m, 1H), 6.39 (m, 1H), 4.59 (m, 1H), 4.52 (m, 1H), 4.11 (m, 2H), 3.86-3.71 (m, 2H), 3.58 (m, 2H), 3.22 (m, 2H), 2.79-0.88 (m, 15H), 1.24 (t, 3H), 1.15 (s, 9H)

IR: 3271, 2976, 1685, 1647, 1541, 1448, 1257, 1192, 1095, 1055

25 Example 80

Trans-4-amidino-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-(1',1'-dimethylpropyl)-seryl] prolyl]-aminomethylcyclohexane (compound No. 977 of Table 1) hydrochloride

30 NMR (DMSO-d₆)

8.74 (br, 4H), 7.68 (m, 1H), 6.01 (m, 1H), 4.83 (m, 1H), 4.57 (m, 2H), 3.74 (m, 2H), 3.50 (m, 2H), 3.14 (m, 1H), 2.97 (m, 1H), 2.5-0.9 (m, 16H), 1.24 (dd, 6H), 1.09 (s, 6H), 0.81 (t, 3H)

IR: 3314, 2978, 1693, 1641, 1543, 1450, 1375, 1261, 1111, 1059

35 Example 81

Trans-4-amidino-[(S)-N-[(R)-N'-ethoxycarbonyl-O-(1',1'-dimethylpropyl)-seryl] prolyl]-aminomethylcyclohexane (compound No. 978 of Table 1) hydrochloride

40 NMR (DMSO-d₆)

8.75 (br, 4H), 7.55 (m, 1H), 6.40 (m, 1H), 4.52 (m, 2H), 4.13 (m, 2H), 3.88-3.70 (m, 2H), 3.55 (m, 2H), 3.28 (m, 1H), 2.87-2.70 (m, 1H), 2.20-1.20 (m, 14H), 1.27 (t, 3H), 1.09 (s, 6H), 0.81 (t, 3H), 1.10-0.90 (m, 2H)

IR: 3292, 2974, 1689, 1645, 1543, 1448, 1259, 1095, 1055

45 Example 82

Trans-4-amidino-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-(1'-ethyl-1'-methyl-propyl)-seryl] prolyl]-aminomethylcyclohexane (compound No. 979 of Table 1) hydrochloride

50 NMR (DMSO-d₆)

8.78 (s, 2H), 8.69 (s, 2H), 7.55 (br, 1H), 5.99 (br, 1H), 4.84 (m, 1H), 4.54 (m, 2H), 3.71 (m, 2H), 3.49 (m, 2H), 3.20-0.90 (m, 16H), 1.64 (q, 4H), 1.23 (t, 6H), 1.03 (s, 3H), 0.78 (t, 6H)

IR: 3315, 2976, 2934, 1685, 1641, 1543, 1450, 1375, 1261, 1111

Example 83

Trans-4-amidino-[(S)-N-[(R)-N'-ethoxycarbonyl-S-t-butyl-cystinyl]prolyl] aminomethylcyclohexane (compound No. 980 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

8.82 (br, 2H), 8.74 (br, 2H), 7.47 (m, 1H), 6.63 (m, 1H), 4.60-4.40 (m, 2H), 4.20-4.21 (m, 2H), 4.00 (m, 1H), 3.72 (m, 1H), 3.24 (m, 1H), 2.87 (m, 2H), 2.65 (m, 1H), 2.18-1.31 (m, 12H), 1.31 (s, 9H), 1.27 (t, 3H), 1.10-0.90 (m, 2H)

10 IR: 3298, 2932, 1693, 1641, 1541, 1448, 1304, 1257, 1161, 1047

Example 84

Trans-4-amidino-[(S)-N-[(R)-N'-isopropoxycarbonyl-0-(1'-methylcyclopentyl)-seryl] aminomethylcyclohexane (compound No. 981 of Table 1) hydrochloride

15 NMR (DMSO-d₆)

8.79 (br, 4H), 7.64 (m, 1H), 5.97 (m, 1H), 4.83 (m, 1H), 4.55 (m, 2H), 3.76 (m, 2H), 3.52 (m, 2H), 3.15-1.20 (m, 22H), 1.27-1.13 (m, 9H), 1.13-0.95 (m, 2H)

20 IR: 3329, 2934, 1684, 1639, 1541, 1450, 1261, 1182, 1111, 1060, 918

Example 85

Trans-4-amidino-[(S)-N-[(R)-N'-isopropoxycarbonyl-0-t-butyl-threonyl] prolyl] aminomethylcyclohexane (compound No. 982 of Table 1) hydrochloride

25 NMR (DMSO-d₆)

8.74 (m, 4H), 7.80 (m, 1H), 5.66 (m, 1H), 4.85 (m, 1H), 4.57 (m, 1H), 4.29 (m, 1H), 3.80-3.60 (m, 3H), 3.05 (m, 2H), 2.60 (m, 1H), 2.50-1.20 (m, 11H), 1.27-1.22 (m, 15H), 1.15 (d, 3H), 1.10-0.90 (m, 2H)

30 IR: 3331, 2978, 1697, 1639, 1543, 1450, 1375, 1265, 1182, 1111

Example 86

Trans-4-amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-3-isopropylthio-3-methyl-butanoyl] aminomethylcyclohexane (compound No. 983 of Table 1) hydrochloride

35 NMR (DMSO-d₆)

9.13 (br, 2H), 8.46 (br, 2H), 7.30 (m, 1H), 5.85 (m, 1H), 4.55 (m, 1H), 4.36 (m, 1H), 4.15-3.85 (m, 3H), 3.69 (m, 1H), 3.02 (m, 2H), 2.30 (m, 1H), 2.00-1.20 (m, 13H), 1.48 (s, 3H), 1.33 (s, 3H), 1.30-1.20 (m, 9H), 1.05-0.85 (m, 2H)

40 IR: 3420, 2974, 1635, 1556, 1521, 1448, 1385, 1298, 1259, 1060

According to the same procedures as that described in Example 24, the following compounds of Examples 87 to 113 were synthesized.

45 Example 87

4-[(S)-N-[(R)-2-hydroxy-cyclohexylacetyl] prolyl] aminomethylbenzamidoxime (compound No. 391 of Table 1)

50 NMR (DMSO-d₆)

9.55 (br, 1H), 8.31 (t, 1H), 7.59 (d, 2H), 7.24 (d, 2H), 5.73 (br, 2H), 4.57 (m, 1H), 4.26-4.32 (m, 3H), 3.91 (br, 1H), 3.40-3.60 (m, 2H), 2.05-0.80 (m, 15H)

IR: 3375, 2926, 2853, 1638, 1561, 1451, 1385, 1244

Example 88

4-[(S)-N-[(R)-N'-isopropoxycarbonyl-phenylalanyl] prolyl] aminomethylbenzamidoxime (compound No. 395 of Table 1)

NMR (CDCl₃)

7.65 (br, 1H), 7.53 (d, 2H), 7.29-7.19 (m, 8H), 5.89 (d, 2H), 5.01 (br, 2H), 4.58-4.45 (m, 4H), 4.27 (dd, 1H), 3.65 (br, 1H), 3.10-2.93 (m, 2H), 2.58 (q, 1H), 2.17 (br, 1H), 1.90-1.50 (m, 2H), 1.11 (d, 4H), 0.96 (d, 2H)

IR: 3331, 2980, 2880, 2365, 1639, 1539, 1452, 126

Example 89

4-[(S)-N-[(R)-2-ethoxycarbonylamino-phenylacetyl] prolyl] aminomethylbenzamidoxime (compound No. 403 of Table 1)

NMR (CDCl₃)

7.60 (br, 1H), 7.47 (d, 2H), 7.40-7.14 (m, 8H), 6.11 (dd, 1H), 5.43 (dd, 1H), 4.96 (br, 2H), 4.70-4.54 (m, 2H), 4.50-4.20 (m, 1H), 4.15-4.00 (m, 1H), 4.00-3.80 (m, 2H), 3.25-3.19 (m, 1H), 2.30-1.80 (m, 4H), 1.16 (dt, 3H)

IR: 3339, 2980, 2365, 1641, 1524, 1437, 1385, 1057

Example 90

25 4-[(S)-N-[(R)-N'-ethoxycarbonyl-valyl]prolyl] aminomethylbenzamidoxime (compound No. 407 of Table 1)

NMR (CDCl₃)

7.57 (br, 1H), 7.54 (d, 2H), 7.20 (d, 2H), 5.98 (d, 1H), 4.97 (br, 2H), 4.68-4.59 (m, 2H), 4.24 (dd, 1H), 4.07 (t, 1H), 4.10-4.00 (m, 1H), 3.90-3.80 (m, 1H), 3.60-3.45 (m, 2H), 2.31 (br, 1H), 2.20-1.95 (m, 4H) 1.88 (d, 1H), 1.01 (t, 3H), 0.97 (d, 6H)

IR: 3337, 2971, 2878, 2363, 1640, 1539, 1445, 1277, 1238

Example 91

35 4-[(S)-N-[(R)-2-ethoxycarbonylamino-3,3-dimethylbutanoyl] prolyl] aminomethylbenzamidoxime (compound No. 409 of Table 1)

NMR (DMSO-d⁶)

8.01 (br, 1H), 7.59 (d, 2H), 7.21 (d, 2H), 7.19-7.15 (m, 1H), 5.73 (br, 2H), 4.36-4.24 (m, 4H), 4.0-3.60 (m, 4H), 2.10-1.80 (m, 5H), 1.06 (t, 3H), 0.96 (s, 9H)

IR: 3345, 2966, 2364, 1647, 1535, 1443, 1240

Example 92

45 4-[(S)-N-[(R)-2-ethoxycarbonylamino-heptanoyl] prolyl] aminomethylbenzamidoxime (compound No. 411 of Table 1)

NMR (CDCl₃)

7.63 (m, 1H), 7.51 (d, 2H), 7.20 (d, 2H), 5.85 (d, 2H), 4.99 (br, 1H), 4.67-4.58 (m, 2H), 4.35-4.28 (m, 2H), 3.99 (br, 1H), 3.86-3.80 (m, 1H), 3.58-3.50 (m, 2H), 2.31 (br, 1H), 2.07-1.90 (m, 3H), 1.80-1.50 (m, 2H), 1.40-1.10 (m, 5H), 1.03 (t, 3H), 1.01-0.84 (m, 3H)

IR: 3347, 2961, 2363, 2342, 1641, 1541, 1447, 1263, 1049

Example 93

4-[(S)-N-[(R)-2-t-butyloxycarbonylamino-heptanoyl] prolyl] aminomethylbenzamidoxime (compound No. 412 of Table 1)

5

NMR (CDCl₃)

7.74-7.70 (m, 1H), 7.49 (d, 2H), 7.27 (t, 1H), 7.20 (d, 2H), 5.43 (d, 1H), 4.93 (br, 2H), 4.65 (d, 1H), 4.48-4.25 (m, 3H), 3.93 (br, 1H), 3.50 (q, 1H), 2.40-2.30 (m, 1H), 2.10-1.90 (m, 3H), 1.70-1.50 (m, 2H), 1.42-1.21 (m, 13H), 0.92-0.80 (m, 3H)

10 IR: 3337, 2961, 2934, 2363, 1641, 1535, 1449, 1368, 1165

Example 94

4-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl] aminomethylbenzamidoxime (compound No. 418 of Table 1)

15

NMR (CDCl₃)

7.58-7.51 (m, 1H), 7.53 (d, 2H), 7.20 (d, 2H), 5.87 (d, 1H), 5.01 (br, 2H), 4.64-4.56 (m, 2H), 4.40 (q, 1H), 4.26 (dd, 1H), 4.10-4.00 (m, 1H), 3.84-3.78 (m, 1H), 3.53-3.47 (m, 2H), 2.32 (br, 1H), 2.10-1.90 (m, 3H), 1.61 (d, 2H), 1.00 (t, 3H), 0.97 (s, 9H)

20 IR: 3324, 2957, 2263, 2342, 1642, 1541, 1445, 1248, 1059

Example 95

25 4-[(S)-N-[(R)-N'-(ethoxycarbonylmethyl)oxycarbonyl-phenylalanyl] prolyl] aminomethylbenzamidoxime (compound No. 984 of Table 1)

NMR (CDCl₃)

7.54 (d, 2H), 7.41 (br, 1H), 7.28-7.20 (m, 8H), 6.70 (d, 1H), 5.09 (br, 2H), 4.66 (dd, 1H), 4.60-4.55 (m, 2H), 4.22-4.00 (m, 4H), 4.03 (q, 2H), 3.62 (br, 1H), 3.10-3.02 (m, 2H), 2.60-2.40 (m, 1H), 2.14 (br, 1H), 2.00-1.50 (m, 3H), 1.22 (t, 3H)

IR: 3356, 3063, 2980, 2364, 1717, 1641, 1539, 1451, 1213, 702

Example 96

35

4-[(S)-N-[(R)-2-ethoxycarbonylamino-cyclohexylacetyl] prolyl] aminomethylbenzamidoxime (compound No. 985 of Table 1)

NMR (CDCl₃)

40 7.52 (d, 2H), 7.54-7.50 (m, 1H), 7.20 (d, 2H), 6.03 (br, 1H), 4.97 (br, 2H), 4.68 (q, 2H), 4.22 (dd, 1H), 4.12-4.03 (m, 2H), 3.64-3.47 (m, 1H), 3.20 (s, 3H), 2.32 (br, 1H), 2.05-1.60 (m, 9H), 1.28-0.97 (m, 6H)

IR: 3343, 2928, 2853, 2365, 1639, 1541, 1449, 1260

Example 97

45

4-[(S)-N-[(R)-2-ethoxycarbonylamino-2'-thienylacetyl] prolyl] aminomethylbenzamidoxime (compound No. 986 of Table 1)

NMR (CDCl₃)

50 7.80-7.60 (m, 1H), 7.46 (dd, 2H), 7.40-6.95 (m, 5H), 6.13 (dd, 1H), 5.71 (dd, 1H), 4.99 (br, 2H), 4.75-4.20 (m, 3H), 4.00-3.80 (m, 2H), 3.70-3.50 (m, 1H), 3.40-3.30 (m, 1H), 2.40-1.80 (m, 4H), 1.16 (dt, 3H)

IR: 3337, 2978, 2364, 1641, 1524, 1443, 1240, 1057, 710

55

• Example 98

4-[(S)-N-[(R)-2-ethoxycarbonylamino-4'-fluorophenylacetyl] prolyl] aminomethylbenzamidoxime (compound No. 987 of Table 1)

5 NMR (CDCl₃)

7.80 (t, 1H), 7.46-7.27 (m, 4H), 7.19-6.92 (m, 4H), 6.19-6.15 (m, 1H), 5.50 (dd, 1H), 5.02 (br, 2H), 4.70-4.20 (m, 3H), 4.10-3.70 (m, 4H), 3.22-3.15 (m, 1H), 2.25-1.80 (m, 4H), 1.16 (dt, 3H)

IR: 3345, 3073, 2980, 2363, 2344, 1641, 1510, 1143

10 Example 99

4-[(S)-N-[(R)-N'-benzyloxycarbonyl-phenylalanyl] prolyl] aminomethylbenzamidoxime (compound No. 988 of Table 1)

15 NMR (CDCl₃)

7.50 (d, 2H), 7.49-7.30 (m, 1H), 7.26-7.12 (m, 12H), 6.40-6.10 (m, 1H), 4.85 (br, 2H), 4.90-4.70 (m, 1H), 4.55-4.40 (m, 4H), 4.30-4.20 (m, 1H), 3.70-3.60 (m, 1H), 3.03-2.95 (m, 1H), 2.20-2.15 (m, 1H), 2.00-1.45 (m, 3H)

20 Example 100

4-[(S)-N-(R)-2-t-butyloxycarbonylamino-4,4-dimethylpentanoyl] prolyl] aminomethylbenzamidoxime (compound No. 989 of Table 1)

25 NMR (CDCl₃)

7.67 (t, 1H), 7.53 (d, 2H), 7.22 (d, 2H), 5.34 (d, 1H), 4.91 (br, 2H), 4.65 (d, 1H), 4.42-4.34 (m, 3H), 4.00-3.90 (m, 1H), 3.48 (q, 1H), 2.40-2.30 (m, 1H), 2.02-1.95 (m, 3H), 1.56-1.53 (m, 2H), 1.31 (s, 9H), 0.98 (s, 9H)

30 IR: 3345, 2959, 2367, 1641, 1535, 1446, 1367, 1167

Example 101

4-[(S)-N-[(R)-N'-dimethylcarbamoyl-phenylalanyl] prolyl] aminomethylbenzamidoxime (compound No. 990 of Table 1)

35 NMR (DMSO-d₆)

9.56 (s, 1H), 8.11 (t, 1H), 7.56 (d, 2H), 7.18 (d, 2H), 7.29-7.16 (m, 5H), 6.70 (d, 1H), 5.74 (br, 2H), 4.40-4.05 (m, 4H), 2.94 (d, 2H), 2.93-2.70 (m, 2H), 2.60 (s, 6H), 1.90-1.60 (m, 4H)

40 IR: 3306, 2932, 2880, 2363, 2341, 1634, 1541, 1453

Example 102

4-[(S)-N-[(S)-N'-benzyloxycarbonyl-β-t-butylaspartyl] prolyl] aminomethylbenzamidoxime (compound No. 991 of Table 1)

45 NMR (CDCl₃)

7.63 (br, 1H), 7.51 (d, 2H), 7.33-7.26 (m, 5H), 7.18 (d, 2H), 6.07 (d, 1H), 5.08 (dd, 2H), 4.92 (br, 2H), 4.90-4.70 (m, 1H), 4.66 (d, 1H), 4.40 (d, 2H), 3.90-3.80 (m, 2H), 3.0-2.90 (m, 1H), 2.55 (dd, 1H), 2.35-2.20 (m, 1H), 2.08-1.90 (m, 3H), 1.25 (s, 9H)

50 IR: 3364, 3063, 2978, 2363, 2343, 2343, 1717, 1641, 1539, 1450, 1369, 1253, 1157

Example 103

Trans-4-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-butoxy-seryl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 485 of Table 1)

5

NMR (CDCl₃)

7.16 (m, 1H), 5.53 (m, 1H), 4.60-4.53 (m, 2H), 4.47 (s, 2H), 4.13-4.06 (m, 2H), 3.76 (br, 2H), 3.60-3.50 (m, 2H), 3.07 (br, 2H), 2.41 (m, 2H), 2.04-1.20 (m, 12H), 1.27 (t, 3H), 1.16 (s, 9H), 1.03-0.94 (m, 2H)
IR: 3352, 2930, 1701, 1651, 1541, 1448, 1259, 1053, 754

10

Example 104

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-t-butylseryl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 486 of Table 1)

15

NMR (CDCl₃)

7.19 (m, 1H), 5.40 (d, 1H), 4.87 (m, 1H), 4.61-4.53 (m, 2H), 4.47 (br, 2H), 3.75 (m, 2H), 3.60-3.40 (m, 2H), 3.08 (t, 2H), 2.40 (m, 1H), 2.20-1.20 (m, 12H), 1.21 (dd, 6H), 1.19 (s, 9H), 1.10-0.90 (m, 2H)
IR: 3356, 2976, 1697, 1649, 1541, 1448, 1261, 1190, 1109, 1022

20

Example 105

Trans-4-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-(1',1'-dimethylpropyl)seryl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 487 of Table 1)

25

NMR (CDCl₃)

7.14 (m, 1H), 5.51 (d, 1H), 4.60-4.50 (m, 2H), 4.48 (br, 2H), 4.09 (m, 2H), 3.78 (m, 2H), 3.55-3.45 (m, 2H), 3.06 (m, 2H), 2.35 (m, 1H), 2.20-0.90 (m, 16H), 1.24 (t, 3H), 1.10 (s, 6H), 0.82 (t, 3H)
IR: 3346, 2976, 2930, 1649, 1543, 1448, 1261, 1176, 1095, 1055

30

Example 106

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-(1',1'-dimethylpropyl)-seryl] aminomethylcyclohexanecarboxamidoxime (compound No. 488 of Table 1) prolyl]-

35

NMR (CDCl₃)

7.18 (m, 1H), 5.38 (d, 1H), 4.86 (m, 1H), 4.61-4.50 (m, 2H), 4.47 (br, 2H), 3.77 (m, 2H), 3.57-3.42 (m, 2H), 3.06 (t, 2H), 2.39 (m, 1H), 2.20-0.90 (m, 16H), 1.23 (dd, 6H), 1.10 (s, 6H), 0.82 (t, 3H)
IR: 3346, 2976, 1703, 1651, 1541, 1448, 1263, 1178, 1109, 1030

40

Example 107

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-(1'-ethyl-1'-methyl-propyl)-seryl] aminomethylcyclohexanecarboxamidoxime (compound No. 490 of Table 1) prolyl]-

45

NMR (CDCl₃)

7.17 (br, 1H), 5.35 (br, 1H), 4.86 (m, 1H), 4.60-4.50 (m, 2H), 4.47 (br, 2H), 3.78 (m, 2H), 3.53-3.38 (m, 2H), 3.07 (t, 2H), 2.37-1.20 (m, 17H), 1.23 (t, 6H), 1.06 (s, 3H), 1.06-0.82 (m, 2H), 0.79 (t, 6H)
IR: 3350, 2976, 2932, 1651, 1541, 1450, 1375, 1263, 1109, 1026

50

Example 108

Trans-4-[(S)-N-[(R)-N'-ethoxycarbonyl-S-t-butylycystinyl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 492 of Table 1)

55

NMR (CDCl₃)

7.27 (m, 1H), 5.81 (m, 1H), 4.60-4.40 (m, 2H), 4.88 (br, 2H), 4.11 (m, 2H), 3.87 (m, 1H), 3.68 (m, 1H), 3.06 (m, 2H), 2.90-2.70 (m, 2H), 2.37 (m, 1H), 2.10-1.20 (m, 12H), 1.32 (s, 9H), 1.25 (t, 3H), 1.10-0.90 (m,

2H)
IR: 3346, 2930, 1699, 1649, 1541, 1448, 1257, 1163, 1051, 929

Example 109

5 Trans-4-[(S)-N-[(R)-2-ethoxycarbonylamino-3-isopropylthio-3-methylbutanoyl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 497 of Table 1)

10 NMR (CDCl₃)
7.16 (m, 1H), 5.62 (m, 1H), 4.61 (d, 1H), 4.47 (br, 2H), 4.35 (d, 1H), 4.12 (m, 2H), 3.96 (m, 1H), 3.76 (m, 1H), 3.10 (m, 1H), 3.00 (m, 2H), 2.38 (m, 1H), 2.00-1.20 (m, 12H), 1.47 (s, 3H), 1.40 (s, 3H), 1.33-1.25 (m, 9H), 1.00-0.90 (m, 2H)
IR: 3354, 2928, 1653, 1541, 1446, 1367, 1302, 1251, 1155, 1055

15 Example 110

Trans-4-[(S)-N-[(S)-N'-t-butyloxycarbonyl-seryl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 992 of Table 1)

20 NMR (CDCl₃)
7.76 (br, 1H), 6.10 (br, 1H), 5.40 (br, 1H), 4.60 (br, 4H), 3.96 (br, 4H), 3.16-1.21 (m, 15H), 1.40 (s, 9H), 0.99 (br, 2H)
IR: 3314, 2978, 1691, 1639, 1541, 1450, 1367, 1165, 1049

25 Example 111

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-t-butyl-threonyl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 993 of Table 1)

30 NMR (CDCl₃)
7.24 (m, 1H), 5.43 (d, 1H), 4.85 (m, 1H), 4.57 (d, 1H), 4.47 (br, 2H), 4.23 (t, 1H), 3.92 (t, 1H), 3.80-3.70 (m, 2H), 3.06 (m, 2H), 2.36 (m, 1H), 2.00-1.20 (m, 12H), 1.23 (s, 9H) 1.23 (dd, 6H), 1.15 (d, 3H), 1.10-0.90 (m, 2H)
IR: 3354, 2978, 1699, 1649, 1543, 1448, 1373, 1257, 1192, 1111, 1032

35 Example 112

Trans-4-[(S)-N-[(R)-2-acetoxy-cyclohexylacetyl] prolyl] aminomethylcyclohexanecarboxamidoxime (compound No. 994 of Table 1)

40 NMR (CDCl₃)
6.80 (br, 1H), 4.61 (t, 2H), 4.49 (br, 2H), 3.90-3.84 (m, 1H), 3.51-3.40 (m, 1H), 3.10-2.85 (m, 2H), 2.38 (br, 1H), 2.11 (s, 3H), 2.06-0.80 (m, 25H)
IR: 3484, 3389, 2928, 2855, 1725, 1649, 1451, 1250

45 Example 113

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-(1'-methylcyclopentyl)-seryl] prolyl]-aminomethylcyclohexanecarboxamidoxime (compound No. 995 of Table 1)

50 NMR (CDCl₃)
7.18 (m, 1H), 5.42 (m, 1H), 4.85 (m, 2H), 4.60-4.49 (m, 4H), 3.73 (m, 2H), 3.57-3.42 (m, 2H), 3.08 (m, 1H), 2.40 (m, 1H), 2.04-1.20 (m, 21H), 1.27-1.20 (m, 9H), 1.03-0.94 (m, 2H)
IR: 3356, 2932, 1695, 1653, 1541, 1448, 1263, 1111, 1030, 918

55 According to the same procedures as that described in Example 48, the following compounds of Examples 114 to 122 were synthesized.

Example 114

Trans-4-[(S)-N-[(R)-2-t-butyloxycarbonylamino-4,4-dimethylpentanoyl] aminomethylcyclohexanecarboxamide O-methoxycarbonyloxime (compound No. 533 of Table 1) prolyl]-

5 NMR (CDCl₃)

7.14 (br, 1H), 5.04 (d, 1H), 4.74 (br, 1H), 4.58 (d, 1H), 4.40-4.30 (m, 1H), 4.00-3.85 (m, 1H), 3.94 (s, 3H),
3.46 (q, 1H), 3.30-3.20 (m, 1H), 2.95-2.88 (m, 1H), 2.42 (br, 1H), 2.26 (t, 1H), 2.00-1.73 (m, 11H), 1.54-1.26
(m, 4H), 1.43 (s, 9H), 1.00 (s, 9H)

10 IR: 3347, 2955, 2870, 1765, 1645, 1539, 1443, 1254, 1169, 879

Example 115

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-leucyl] prolyl] aminomethylcyclohexanecarboxamide O-methox-
75 ycarbonyloxime (compound No. 540 of Table 1)

NMR (CDCl₃)

7.11 (br, 1H), 5.18 (d, 1H), 4.90-4.70 (m, 1H), 4.77 (br, 2H), 4.56 (d, 1H), 4.40-4.30 (m, 1H), 3.95-3.86
(m, 1H), 3.85 (s, 3H), 3.46 (q, 1H), 3.20-2.95 (m, 2H), 2.40-2.30 (m, 1H), 2.30-2.10 (m, 1H), 2.00-1.20 (m,
20 13H), 1.23 (dd, 6H), 1.04-0.89 (m, 8H)

IR: 3354, 2957, 2932, 2872, 2363, 2341, 1763, 1643, 1541, 1443, 1260

Example 116

25 Trans-4-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-butyl-seryl] prolyl] aminomethylcyclohexanecarboxamide O-
methoxycarbonyloxime (compound No. 996 of Table 1)

NMR (CDCl₃)

7.20 (m, 1H), 5.34 (m, 1H), 4.70 (s, 2H), 4.61 (m, 1H), 4.50 (m, 1H), 4.12-4.06 (m, 2H), 3.85 (s, 3H), 3.74
30 (m, 2H), 3.60-3.39 (m, 2H), 3.06 (m, 2H), 2.41-1.20 (m, 13H), 1.25 (t, 3H), 1.16 (s, 9H), 1.08-0.94 (m, 2H)
IR: 3348, 2976, 1768, 1703, 1645, 1541, 1442, 1255, 1053, 879, 752

Example 117

35 Trans-4-[(S)-N-[(R)-2-hydroxy-4-methyl-pentanoyl] prolyl] aminomethylcyclohexanecarboxamide O-methox-
ycarbonyloxime (compound No. 997 of Table 1)

NMR (CDCl₃)

7.07 (m, 1H), 4.73 (br, 2H), 4.52 (d, 1H), 4.23 (m, 4H), 3.56 (m, 1H), 3.40 (m, 1H), 3.13 (m, 3H), 2.41 (m,
40 1H), 2.30-0.90 (m, 15H), 1.33 (t, 3H), 0.97 (dd, 6H)
IR: 3346, 2932, 1759, 1641, 1450, 1369, 1251, 1078, 920, 846

Example 118

45 Trans-4-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-butyl-seryl] prolyl] aminomethylcyclohexanecarboxamide O-ac-
etylloxime (compound No. 998 of Table 1)

NMR (CDCl₃)

7.20 (m, 1H), 5.33 (m, 1H), 4.69 (s, 2H), 4.60 (m, 1H), 4.51 (m, 1H), 4.17-4.07 (m, 2H), 3.77-3.65 (m,
50 2H), 3.60-3.46 (m, 2H), 3.09-3.08 (m, 2H), 2.40-1.00 (m, 13H), 2.15 (s, 3H), 1.25 (t, 3H), 1.16 (s, 9H), 1.14-
0.94 (m, 2H)
IR: 3346, 2976, 1641, 1541, 1448, 1234, 1053, 754

Example 119

Trans-4-[(S)-N-[(R)-N'-isopropoxycarbonyl-O-t-butyl-seryl] prolyl] aminomethylcyclohexanecarboxamide O-methoxycarbonyloxime (compound No. 999 of Table 1)

5 NMR (CDCl₃)
7.23 (t, 1H), 5.26 (d, 1H), 4.85 (m, 1H), 4.71 (m, 1H), 4.59 (d, 1H), 4.49 (m, 1H), 3.85 (s, 3H), 3.73 (m, 2H), 3.61-3.49 (m, 2H), 3.06 (t, 2H), 2.36 (m, 1H), 2.26 (t, 3H), 2.10-2.20 (m, 11H), 1.21 (dd, 6H), 1.16 (s, 9H), 1.10-0.90 (m, 2H)

10 IR: 3348, 2978, 1768, 1703, 1649, 1541, 1444, 1259, 1192, 1109

Example 120

15 4-N-ethoxycarbonyl-amidino-[(S)-N-[(R)-2-methylsulfonylamino-4,4-dimethylpentanoyl] prolyl]-aminomethylbenzene (compound No. 1000 of Table 1)

NMR (CDCl₃)
7.29 (d, 2H), 7.30 (d, 2H), 7.23 (t, 1H), 5.53 (br, 1H), 4.52-4.37 (m, 2H), 4.24-4.17 (m, 2H), 4.20 (q, 2H), 3.90-3.80 (m, 1H), 3.50-3.40 (m, 1H), 2.77 (s, 3H), 2.28-2.20 (m, 4H), 1.84 (br, 2H), 1.60-1.40 (m, 2H), 1.34 (t, 3H), 1.02 (s, 9H)

20 IR: 3378, 2957, 2876, 2364, 2230, 1628, 1267, 1147

Example 121

25 4-N-methoxycarbonyl-amidino-[(S)-N-[(R)-2-methylsulfonylamino-4,4-dimethylpentanoyl] prolyl]-aminomethylbenzene (compound No. 1001 of Table 1)

NMR (CDCl₃)
7.78 (d, 2H), 7.29 (d, 2H), 7.27 (t, 1H), 5.49 (d, 1H), 4.56 (d, 1H), 4.42 (dq, 2H), 3.77 (s, 3H), 3.80-3.70 (m, 2H), 3.60-3.51 (m, 1H), 2.79 (s, 3H), 2.28-1.60 (m, 12H), 1.20-0.95 (m, 5H)

30 IR: 3376, 2930, 2855, 2365, 1626, 1528, 1501, 1439, 1271, 1144

Example 122

35 Trans-4-N-methoxycarbonyl-amidino-[(S)-N-[(R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl] prolyl]-aminomethylcyclohexane (compound No. 599 of Table 1)

NMR (CDCl₃)
7.08 (br, 1H), 5.17 (d, 1H), 4.56 (d, 1H), 4.50-4.40 (m, 1H), 4.20-3.80 (m, 3H), 3.70 (s, 3H), 3.47 (q, 1H), 3.20-3.00 (m, 2H), 2.45-2.30 (m, 1H), 2.20-1.30 (m, 15H), 1.24 (t, 3H), 0.99 (s, 9H), 1.10-0.89 (m, 2H)

40 IR: 3366, 2953, 2365, 1780, 1697, 1640, 1533, 1441, 1271, 1055

According to the same procedures as that described in Example 52, the following compounds of Examples 123 to 125 were synthesized.

45 Example 123

Trans-4-amino-[(S)-N-[(R)-2-carboxymethylsulfonylamino-heptanoyl]prolyl]aminomethylcyclohexane (compound No. 791 of Table 1) hydrochloride

50 NMR (DMSO-d₆)
7.97 (m, 2H), 7.57 (m, 1H), 4.19 (m, 2H), 4.01 (d, 1H), 3.80 (d, 1H), 3.68 (m, 1H), 3.50 (m, 1H), 2.88 (m, 3H), 2.04 (m, 1H), 1.90 (m, 5H), 1.73 (m, 4H), 1.58-1.13 (m, 12H), 1.00-0.84 (m, 5H)

55 IR: 3387, 2934, 1726, 1637, 1553, 1452, 1325, 1159, 1090, 1046, 604

Example 124

Trans-4-amino-[(S)-N-[(R)-N'-methylsulfonyl-O-methytyrosyl] prolyl] aminomethylcyclohexane (compound No. 1002 of Table 1) hydrochloride

5 NMR (DMSO-d₆)

8.10 (br, 3H), 7.77 (t, 1H), 7.67 (d, 1H), 7.17 (d, 2H), 6.87 (d, 2H), 4.25-4.16 (m, 1H), 3.75 (br, 2H), 3.73 (s, 3H), 3.57-3.40 (m, 1H), 3.00-2.70 (m, 5H), 2.77 (s, 3H), 2.00-1.71 (m, 8H), 1.40-1.20 (m, 3H), 1.00-0.80 (m, 2H)

10 IR: 3385, 2936, 2363, 1639, 1514, 1450, 1304, 1248, 1149

Example 125

Trans-4-amino-[(S)-N-[(R)-N'-ethoxycarbonyl-O-t-butyloxy-seryl] prolyl] aminomethylcyclohexane (compound No. 1003 of Table 1) hydrochloride

15 NMR (DMSO-d₆)

8.29 (s, 3H), 7.20 (s, 1H), 5.69 (d, 1H), 4.58-4.47 (m, 2H), 4.12 (m, 2H), 3.82 (m, 1H), 3.61-3.48 (m, 2H), 3.09 (m, 2H), 2.32-0.86 (m, 15H), 1.27 (t, 3H), 1.16 (s, 9H)

20 IR: 3358, 2974, 1645, 1541, 1448, 1257, 1192, 1053

According to the same procedures as that described in Example 67, the following compounds 126 to 130 were synthesized.

Example 126

25 Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-2-hydroxy-cyclohexylacetyl] prolyl]-aminomethylcyclohexane (compound No. 966 of Table 1)

NMR (CDCl₃)

30 7.08 (m, 1H), 4.54 (d, 1H), 4.06 (m, 1H), 3.59 (m, 1H), 3.49 (s, 2H), 3.46 (m, 1H), 3.07 (m, 2H), 2.48 (m, 2H), 2.11 (s, 3H), 2.01 (m, 2H), 1.90-1.70 (m, 10H), 1.58 (m, 3H), 1.41-0.94 (m, 10H)
IR: 3387, 2928, 2855, 1821, 1736, 1638, 1543, 1451, 1387, 1223, 1107, 999, 712

Example 127

35 Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-N'-methylsulfonyl-phenylalanyl] prolyl]-aminomethylcyclohexane (compound No. 967 of Table 1)

NMR (CDCl₃)

40 7.35-7.20 (m, 5H), 6.71 (t, 1H), 5.48 (d, 1H), 4.44 (m, 1H), 4.25 (m, 1H), 3.60 (m, 1H), 3.48 (s, 2H), 3.09 (m, 1H), 2.96 (m, 3H), 2.78 (s, 3H), 2.77 (m, 1H), 2.50 (m, 1H), 2.20 (m, 1H), 2.11 (s, 3H), 1.88-1.56 (m, 8H), 1.42 (m, 1H), 1.24 (m, 2H), 0.96 (m, 2H)
IR: 3387, 2930, 1819, 1736, 1649, 1541, 1499, 1451, 1318, 1223, 1152, 999

45 Example 128

Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-2-ethoxycarbonylamino-cyclohexylacetyl] prolyl]aminomethylcyclohexane (compound No. 1004 of Table 1)

50 NMR (CDCl₃)

7.11 (m, 1H), 5.31 (m, 1H), 4.58 (d, 1H), 4.10 (t, 2H), 4.04 (m, 1H), 3.94 (m, 1H), 3.56 (m, 1H), 3.49 (s, 2H), 3.04 (m, 2H), 2.52 (m, 1H), 2.36 (m, 2H), 2.12 (s, 3H), 2.00 (m, 3H), 1.92-1.62 (m, 10H), 1.43 (m, 2H), 1.25 (q, 3H), 1.22 (m, 4H), 1.06 (m, 4H)
IR: 3353, 2930, 2855, 1823, 1653, 1537, 1449, 1223, 1040, 999, 772, 627

Example 129

Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-2-isopropoxyamino-4,4-dimethyl-pentanoyl]prolyl]aminomethylcyclohexane (compound No. 1005 of Table 1)

NMR (CDCl₃)

7.10 (m, 1H), 5.07 (d, 1H), 4.83 (m, 1H), 4.57 (d, 1H), 4.40 (m, 1H), 3.96 (m, 1H), 3.48 (s, 2H), 3.45 (m, 2H), 3.04 (m, 2H), 2.50 (m, 1H), 2.39 (m, 1H), 2.11 (s, 3H), 2.00 (m, 3H), 1.83 (m, 3H), 1.69 (m, 5H), 1.57-1.42 (m, 3H), 1.25 (d, 3H), 1.22 (d, 3H), 1.00 (s, 9H)

IR: 3349, 2934, 2872, 1823, 1653, 1537, 1445, 1225, 1047, 999, 712, 627

Example 130

Trans-4-(5-methyl-1,3-dioxo-2-on-4-ylmethyl)amino-[(S)-N-[(R)-2-methylsulfonylamino-cyclohexylacetyl]prolyl]aminomethylcyclohexane (compound No. 1006 of Table 1)

NMR (CDCl₃)

6.69 (t, 1H), 5.26 (d, 1H), 3.82 (m, 2H), 3.54 (m, 2H), 3.49 (s, 2H), 3.13 (m, 1H), 3.00 (m, 1H), 2.96 (s, 3H), 2.51 (m, 1H), 2.30 (m, 1H), 2.11 (s, 3H), 2.02 (m, 4H), 1.80 (m, 9H), 1.61 (m, 2H), 1.43 (m, 1H), 1.20 (m, 5H), 0.97 (m, 3H)

IR: 3376, 2930, 2855, 1642, 1536, 1451, 1352, 1154, 984, 760, 619, 517

Experimental Example 1: Determination of antithrombin activity

25 (i) The measuring method for hydrolysis inhibition of synthetic substrate (S-2238)

S-2238 (manufactured by Kabi Co.) is dissolved in a Tris hydrochloric acid buffer solution (pH: 8.3) to prepare a S-2238-0.4 M Tris hydrochloric acid solution having a concentration of 80 μ M. To 175 μ l of the solution, an aqueous solution of a compound of the present invention (515 μ l) is added. After incubating at 30 37°C for one minute, 10 μ l of a bovine thrombin solution (4.4 units/ml, manufactured by Mochida Co., Ltd.) is added. A hydrolysis reaction rate of the substrate is determined by measuring a change in absorbance of 405 nm at 37°C.

The inhibitor concentration exhibiting an absorbance which is half as large as that obtained in case of adding no inhibitor (compound of the present invention) was determined as I_{50} (μ M).

35 (ii) The measuring method for coagulation inhibition of rat plasma

The compound of the present invention is dissolved in water or saline to form a solution of a total volume of 0.1 ml. To the solution, 0.1 ml of rat plasma is added and the mixture is incubated at 37°C for 30 40 seconds. Then, 0.1 ml of bovine thrombin (8 units/ml, Mochida Co., Ltd.) is added and the coagulation time is measured at 37°C. The concentration of the inhibitor (i.e., the compound of the present invention) which doubles the coagulation time that obtained in the absence of the inhibitor was determined as I_{50} (μ M).

45 (iii) The measuring method for antithrombin activity of rat plasma on oral administration

To a rat abstained from bait overnight, an aqueous solution or suspension of the present compound (inhibitor) (30 mg/kg) is orally administered using an oral sound.

After one hour, 2 ml of blood is collected from cava abdominalis and the antithrombin activity in plasma is measured using a method of the above item (ii). As a control experiment, the coagulation time of blood 50 collected from a rat which has not been administered the inhibitor was measured. The extension effect on the coagulation time is represented by the numerical value obtained by comparing the data with those obtained in control experiment, wherein the numerical value obtained in the control experiment was assumed to be 1.

Experimental Example 2: Determination of Antitrypsin activity

(i) The measuring method for hydrolysis inhibition of synthetic substrate (S-2222)

5 S-2222 (manufactured by Kabi Co.) is dissolved in a Tris hydrochloric acid (pH: 8.3) to prepare a S-2222-0.4M Tris hydrochloric acid solution having a concentration of 400 μM . To the solution (175 μl), 515 μl of a solution of a compound of the present invention is added. After incubating at 37°C for one minute, 10 μl of a bovine trypsin solution (1 to 2 mg/ml, manufactured by Sigma Co.) is added. A hydrolysis reaction rate of the substrate is determined by measuring a change in absorbance of 405 nm at 37°C.

10 The inhibitor concentration exhibiting an absorbance which is half as large as that obtained in case of adding no inhibitor (compound of the present invention) was determined as I_{50} (μM).

The results are shown in Table 2.

15 Table 2

Antithrombin activity I_{50} (μM)

20	Example No.	Synthetic substrate method	Flat plasma method	Antitrypsin activity I_{50} (μM)	Thrombin coagulation time extension coefficient on oral administration
25	1			0.046	5.97
	2			0.030	8.75
	3			0.027	4.46
	4	0.0076		0.021	0.040
	5			0.048	6.70
30	6			0.056	3.16
	7			0.030	
	8			0.122	
	9			0.11	
	10			0.17	
35	12			0.083	
	13	0.72		0.59	
	15	0.011		0.038	2.2
	16	0.021			1.7
	17	0.015		0.053	3.2
40	18			0.060	
	19			0.031	
	20			0.028	
	21	0.021			1.0
	22	0.014			0.94
45	23	0.017		0.058	3.6
	24				3.28
	25		> 300		2.82
	26				4.16
50	27				3.52
	28				4.35
	30				2.75
	31				2.77
	32				3.58

Antithrombin activity I_{50} (μM)

Example No.	Synthetic substrate method	Human plasma method	Antitrypsin activity I_{50} (μM)	Thrombin coagulation time extension coefficient on oral administration
33				3.99
35				3.72
36				2.85
10 37				4.37
39				2.37
40				2.70
41				2.94
15 42				4.36
43				3.09
46				2.16
47				2.34
48				4.91
20 49				7.12
50				3.50
51				2.80
25 52	0.13	0.045	14	4.10
53	0.081	0.059	1.4	
54		0.23		
56	0.13	0.080	14	2.10
57		0.082		
58		0.097		2.35
30 61		0.056		
62		0.088		2.18
64		0.13		1.25
65				3.67
35 67	0.56	0.081	20	

Experimental Example 3: Acute toxicity test

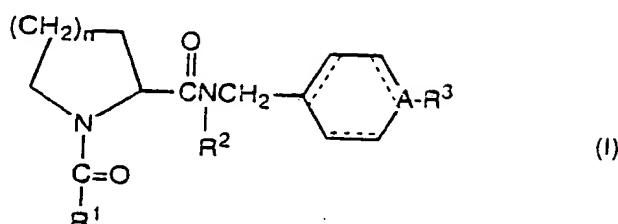
40 Acute toxicity was determined in rat. An approximate lethal dose was determined by conducting an oral acute toxicity test using rats. The results are shown in Table 3.

Table 3

Example No.	Approximate lethal dose mg/kg	
	Male	Female
4	750	1500
52	Not less than 2000	Not less than 2000
33	Not less than 2000	Not less than 2000
37	Not less than 2000	Not less than 2000

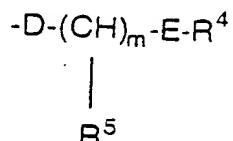
Claims

5 1. A prolineamide derivative represented by the formula (I):



15 wherein A is a carbon atom or a nitrogen atom;
 n is an integer of 0 to 2;
 a broken line is no bond or a single bond;
 R¹ is

20



30 {wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;

35 R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a hydrogen atom, a C₁-C₆ alkyl group, an optionally substituted C₆-C₁₀ aryl group, an optionally substituted C₃-C₈ cycloalkyl group or an optionally substituted C₇-C₁₂ aralkyl group), -SR⁷ (R⁷ is a C₁-C₆ alkyl group, an optionally substituted C₆-C₁₀ aryl group, an optionally substituted C₃-C₈ cycloalkyl group or an optionally substituted C₇-C₁₂ aralkyl group), -SOR⁸ (R⁸ is an optionally substituted C₆-C₁₀ aryl group or an optionally substituted C₃-C₈ cycloalkyl group), -SO₂R⁹ (R⁹ is an optionally substituted C₆-C₁₀ aryl group or an optionally substituted C₃-C₈ cycloalkyl group), -COR¹⁰ (R¹⁰ is a hydroxyl group, a C₁-C₆ alkoxy group, an optionally substituted C₆-C₁₀ aryl group or an optionally substituted C₃-C₈ cycloalkyl group), -NHR¹¹ (R¹¹ is a C₁-C₆ alkyl group, an optionally substituted C₆-C₁₀ aryl group, an optionally substituted C₃-C₈ cycloalkyl group or an optionally substituted C₇-C₁₂ aralkyl group), -NHCOR¹² (R¹² is a C₁-C₆ alkoxy group, an optionally substituted C₆-C₁₀ aryl group, an optionally substituted C₃-C₈ cycloalkyl group or an optionally substituted C₇-C₁₂ aralkyloxy group), -NHSO₂R¹³ (R¹³ is a C₁-C₆ alkyl group, an optionally substituted C₇-C₁₂ aralkyl group, or an optionally substituted 5- to 10-membered heterocyclic group), an optionally substituted 5- to 10-membered heterocyclic group or -SiR¹⁴R¹⁵R¹⁶ (R¹⁴, R¹⁵, and R¹⁶ independently indicate a C₁-C₆ alkyl group);

40 R⁵ is a -OR¹⁷ (R¹⁷ is a hydrogen atom, -SiR²²R²³R²⁴ (R²², R²³, and R²⁴ independently indicate a C₁-C₆ alkyl group), a C₁-C₆ alkyl group, or an optionally substituted 5- to 10-membered heterocyclic group), -OCOR¹⁸ (R¹⁸ is a hydrogen atom, a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, an amino group, a C₁-C₆ alkylamino group, a C₂-C₁₂ dialkylamino group or a C₂-C₇ alkenylamino group), -NHR¹⁹ (R¹⁹ is a hydrogen atom, a C₁-C₆ alkyl group or an optionally substituted C₇-C₁₂ aralkyl group), NHCOR²⁰ (R²⁰ is a hydrogen atom, a C₁-C₆ alkyl group, a C₁-C₆ haloalkyl group, a C₁-C₆ alkoxy group, an optionally substituted C₃-C₈ cycloalkyl group, a C₂-C₇ carboxyalkyloxy group, a C₂-C₇ alkenyloxy group, an alkoxycarbonylalkoxy group, a C₂-C₁₂ dialkylamino group or an optionally substituted C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group, a C₁-C₆ haloalkyl group, a C₂-C₇ carboxyalkyl group, an optionally substituted C₆-C₁₀ aryl group, a C₃-C₉ alkoxycarbonylalkyl group or an optionally

substituted C₇-C₁₂ aralkyl group); and m is 0 or 1};

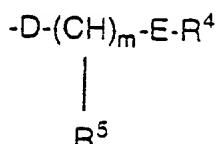
R² is a hydrogen atom or a C₁-C₆ alkyl group; and R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom, a C₁-C₆ alkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₁-C₆ alkoxy group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ alkoxycarbonyloxy group, a hydroxyl group or a C₂-C₇ hydroxyalkylcarbonyloxy group), -NH-C(=NR²⁵)NH₂ (R²⁵ is as defined above) or -NHR²⁶ (R²⁶ is a hydrogen atom, a C₁-C₆ alkyl group, a C₂-C₇ acyl group, a C₂-C₇ alkoxycarbonyl group or a 5-C₁-C₃ alkyl-1,3-dioxol-2-on-4-ylmethyl group); provided that R³ is -C(=NR²⁵)NH₂ (R²⁵ is as defined above) when A is a nitrogen atom, or a salt or hydrate thereof.

10 2. The compound according to claim 1, wherein the 5- to 10-membered heterocyclic group contains 1 to 4 heteroatoms selected from the group consisting of an oxygen atom, a sulfur atom and a nitrogen atom and the total number of atoms constituting the ring is 5 to 10.

15 3. The compound according to claim 1 or 2, wherein the substituent is a group selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ haloalkyl group, a C₁-C₆ alkoxy group, a hydroxyl group, a carboxyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ alkoxycarbonyloxy group, a C₈-C₁₃ aralkyloxycarbonyl group, a C₃-C₉ alkoxycarboxyalkoxy group and a halogen atom.

20 4. The compound according to any one of claims 1 to 3, wherein A is a carbon atom.

5. The compound according to claim 1 or 4, wherein n is 1 or 2; R¹ is



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{wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;

35 R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₁-C₅ alkyl group; a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group; or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group; a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group); or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group);

40 -COOH; a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group; or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group);

45 -COOR⁸ (R⁸ is a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group); or a C₇-C₁₂ aralkyl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a C₁-C₆ alkoxy group, a halogen atom, a hydroxyl group, a carboxyl group, a C₂-C₇ alkoxycarbonyl group, a C₂-C₇ carboxyalkyl group, a C₂-C₇ acyl group, a C₂-C₇ acyloxy group, a C₂-C₇ alkoxycarbonyloxy group, a C₃-C₉ alkoxycarbonylalkoxy group and a benzyloxycarbonyl group);

50 -SiR¹⁴R¹⁵R¹⁶ (R¹⁴, R¹⁵, and R¹⁶ independently indicate a C₁-C₆ alkyl group);

55 R⁵ is -OH, -OCOR¹⁸ (R¹⁸ is a C₁-C₆ alkoxy group or a C₂-C₇ alkenylamino group), -NH₂.

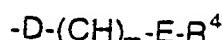
5 -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group, a C₆-C₁₀ aryloxy group, a C₃-C₉ alkoxy carbonylalkoxy group, a C₂-C₁₂ dialkylamino group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group, a C₂-C₇ carboxyalkyl group, a C₆-C₁₀ aryl group, a C₃-C₉ alkoxy carbonylalkyl group or a C₇-C₁₂ aralkyl group); and m is 0 or 1};

R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom, a C₂-C₇ alkoxy carbonyl group or a hydroxyl group),

-NH-C(=NR²⁵)NH₂ (R²⁵ is as defined above) or -NHR²⁵ (R²⁵ is a hydrogen atom, a C₂-C₇ alkoxy carbonyl group or a 5-C₁-C₃ alkyl-1,3-dioxol-2-on-4-ylmethyl group).

10 6. The compound according to claim 1 or 4, wherein n is 1; R¹ is



20 {wherein D and E independently indicate a single bond or an optionally branched C₁-C₆ alkylene group;

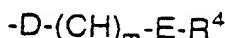
R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group or C₇-C₁₂ aralkyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group); a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group; or a C₃-C₆ cycloalkyl group;

R⁵ is -OH, NH₂, -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₆ alkyl group or a C₆-C₁₀ aryl group); and m is 1};

30 R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

7. The compound according to claim 1 or 4, wherein n is 1; R¹ is



40 {wherein D is a single bond; E is a single bond or a C₁-C₆ alkylene group;

R⁴ is a C₁-C₆ alkyl group; -OR⁶ (R⁶ is a C₆-C₁₀ aryl group which may be substituted with at least one substituent selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group or C₇-C₁₂ aralkyl group); -SR⁷ (R⁷ is a C₁-C₆ alkyl group); a C₆-C₁₀ aryl group which may be substituted with at least one or more substituents selected from the group consisting of a C₁-C₆ alkyl group, a halogen atom, a carboxyl group, a C₂-C₇ carboxyalkyl group and a benzyloxycarbonyl group; or a C₃-C₆ cycloalkyl group;

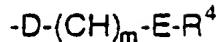
R⁵ is -NH₂, -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group or a C₇-C₁₂ aralkyloxy group) or -NHSO₂R²¹

50 (R²¹ is a C₁-C₆ alkyl group or a C₆-C₁₀ aryl group); and m is 1};

R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

8. The compound according to claim 1, wherein A is a carbon atom; n is 1; R¹ is



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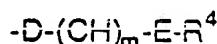
{wherein D is a single bond; E is a single bond or a C₁-C₃ alkylene group; R⁴ is a C₃-C₆ alkyl group, -OR⁶ (R⁶ is a C₁-C₅ alkyl group, a phenyl group, or a C₃-C₆ cycloalkyl group; R⁵ is -OH, -NHR¹⁹ (R¹⁹ is a hydrogen atom), -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group) or -NHSO₂R²¹ (R²¹ is a C₁-C₃ alkyl group); and m is 1};

R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group) or -NH₂.

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9. The compound according to claim 1 or 4, wherein n is 1; R¹ is



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{D is a single bond; E is a single bond or a C₁-C₆ alkylene group; R⁴ is a C₁-C₆ alkyl group; R⁵ is -NHCOR²⁰ (R²⁰ is a C₁-C₆ alkoxy group); and m is 1};

R² is a hydrogen atom; and

R³ is -C(=NR²⁵)NH₂ (R²⁵ is a hydrogen atom or a hydroxyl group).

30 10. Trans-4-[(S)-N-((R)-2-ethoxycarbonylamino-4,4-dimethylpentanoyl) prolyl]aminomethylcyclohexane-carboxamidoxime or a salt or hydrate thereof.

11. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 10 and a pharmaceutically acceptable carrier therefor.

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12. The use of a compound as claimed in any one of claims 1 to 10 in the manufacture of a medicament effective as a protease inhibitor.

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EUROPEAN SEARCH REPORT

Application Number
EP 95 10 1059

DOCUMENTS CONSIDERED TO BE RELEVANT									
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)						
X	CHEMICAL ABSTRACTS, vol. 104, no. 7, 17 February 1986, Columbus, Ohio, US; abstract no. 47665b, * abstract * & SYMP. BIOL. HUNG. (PROTEINASE ACTION), vol.25, 1984, BUDAPEST pages 277 - 298 S. BAJUSZ & CAS REGISTRY HANDBOOK 1986 SUPPL. (STN DATABASE) * RN: 99742-41-3 *	1	C07D207/16 C07D211/60 C07D403/06 C07D403/12 C07D401/12 C07D403/08 C07D403/10 C07K5/06 A61K31/40						
X,P	EP-A-0 601 459 (BRISTOL-MYERS SQUIBB CO.) * see ex. 30,32-35,47,49-53 *	1							
A	CHEMICAL ABSTRACTS, vol. 103, no. 3, 22 July 1985, Columbus, Ohio, US; abstract no. 18900y, * abstract * & BIOCHEMISTRY, vol.24, no.13, 1985, EASTON, PA US pages 3149 - 3157 C.F. VENCILL ET AL.	1							
A	CHEMICAL ABSTRACTS, vol. 92, no. 3, 21 January 1980, Columbus, Ohio, US; abstract no. 17850z, * abstract * & BIOORG. CHEM., vol.8, no.3, 1979 pages 299 - 309 C.H. HASSALL ET AL.	1	C07D C07K A61K						
A	WO-A-93 15756 (CORVAS INTERNATIONAL, INC.) * the whole document *	1							
		-/--							
<p>The present search report has been drawn up for all claims</p> <table border="1"> <tr> <td>Place of search</td> <td>Date of completion of the search</td> <td>Examiner</td> </tr> <tr> <td>BERLIN</td> <td>14 June 1995</td> <td>Frelon, D</td> </tr> </table>				Place of search	Date of completion of the search	Examiner	BERLIN	14 June 1995	Frelon, D
Place of search	Date of completion of the search	Examiner							
BERLIN	14 June 1995	Frelon, D							
CATEGORY OF CITED DOCUMENTS		<p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons A : member of the same patent family, corresponding document</p>							
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p>									



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EUROPEAN SEARCH REPORT

Application Number

EP 95 10 1059

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	US-A-5 153 176 (ABE ET AL.) * the whole document *	1	
D	& JP-A-4 089 498 (NITTO BISEKI CO., LTD.) -----		
TECHNICAL FIELDS SEARCHED (Int.Cl.6)			
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
BERLIN	14 June 1995	Frelon, D	
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone		T : theory or principle underlying the invention	
Y : particularly relevant if combined with another document of the same category		E : earlier patent document, but published on, or after the filing date	
A : technological background		D : document cited in the application	
O : non-written disclosure		L : document cited for other reasons	
P : intermediate document		A : member of the same patent family, corresponding document	

